STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 133847

TO: Rei-Tsang Shiao **Location: 5a10 / 5c18** **Wednesday, September 29, 2004** **Art Unit: 1626** **Phone: 272-0707** **Serial Number: 10 / 692856**	**From: Jan Delaval** **Location: Biotech-Chem Library** **Rem 1A51** **Phone: 272-2504** **jan.delaval@uspto.gov**

Search Notes

Jan Pelgrat
for search

Access DB# 133547

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Robert (Kate) Shiau Examiner #: 79521 Date: 9/28/04
Art Unit: 1626 Phone Number 30 2-0707 Serial Number: 10/692856
Mail Box and Bldg/Room Location: 5A15/5C18 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

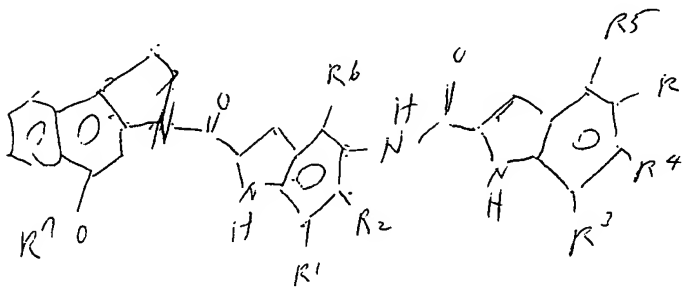
Title of Invention: prodrugs of cc-1065

Inventors (please provide full names): Yongxin

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

I each a cpd of formula (I) & linker
Ia formula (V).



R, R1 ~ R7 are sm.

II method of use of cpd I

III Elected cpd of claim 18

****

STAFF USE ONLY

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Searcher Phone #: 22504
Searcher Location: _____
Date Searcher Picked Up: 9/29
Date Completed: 9/29
Searcher Prep & Review Time: _____
Clerical Prep Time: 15
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Type of Search

NA Sequence (#) _____
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Structure (#) ✓
Bibliographic _____
Litigation _____
Fulltext _____
Patent Family _____
Other _____

Vendors and cost where applicable

STN ✓
Dialog _____
Questel/Orbit _____
Dr.Link _____
Lexis/Nexis _____
Sequence Systems _____
WWW/Internet _____
Other (specify) _____

PTO-1590 (8-01)

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   28 SEP 2004  HIGHEST RN 753424-73-6
DICTIONARY FILE UPDATES:  28 SEP 2004  HIGHEST RN 753424-73-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
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http://www.cas.org/ONLINE/DBSS/registryss.html

=> d sta que l25
L1              STR
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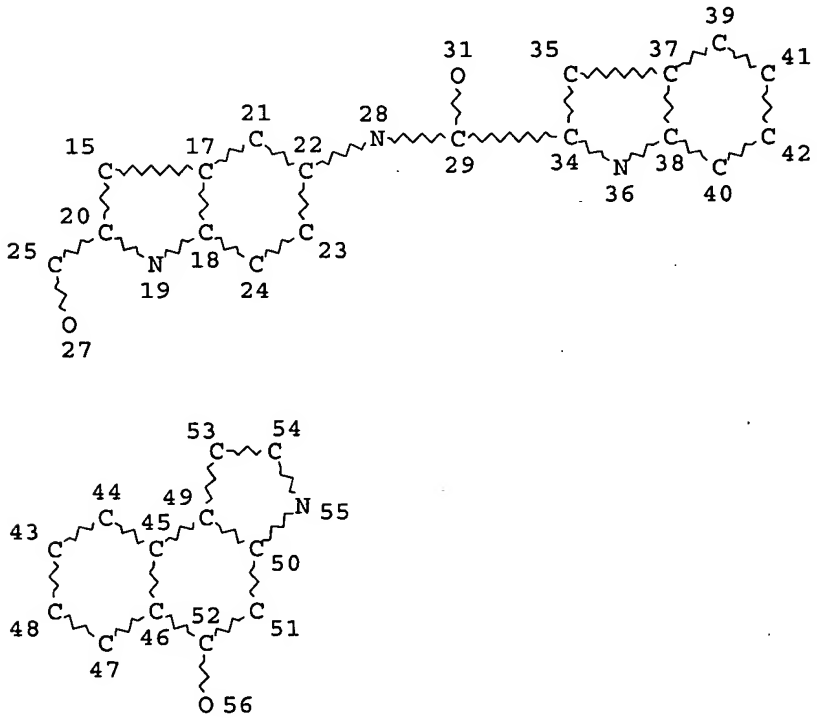

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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STEREO ATTRIBUTES: NONE
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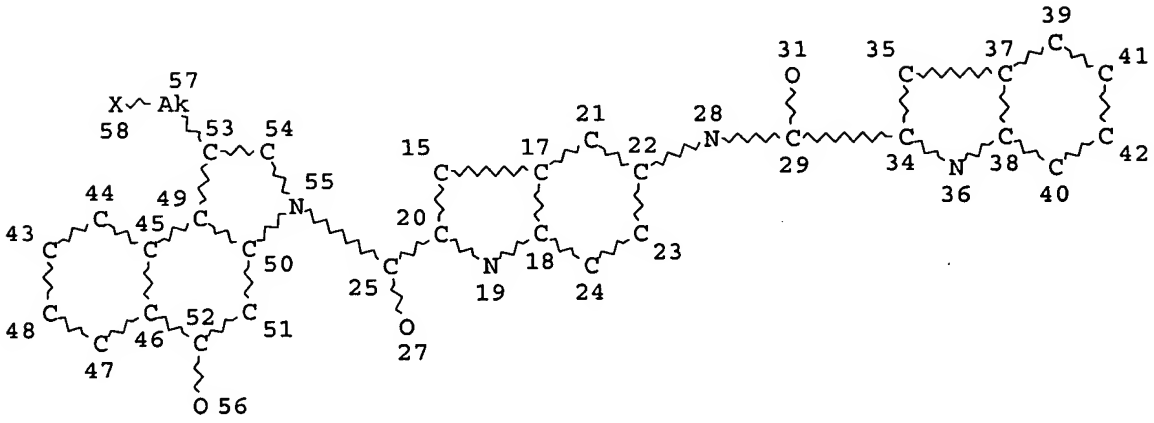
L24 STR



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100.0% PROCESSED 98 ITERATIONS 97 ANSWERS
SEARCH TIME: 00.00.01

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L6 STR L1
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SAV L7 SHIAL692A/A TEMP

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L10 32 S L8,L9
L11 3 S L10 AND (CHARI R? OR YONGXIN R?)/AU
L12 1 S L10 AND ZHAO R?/AU
L13 3 S L10 AND IMMUNOGEN?/PA,CS
L14 3 S L11-L13
SEL HIT RN

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L19           4 S L16 AND (C35H30CLN5O4S2 OR C34H28CLN5O4S OR C35H31CLN5O7PS2 O
L20           5 S L15 AND 9/NR
L21           2 S L20 NOT (9/O OR P/ELS)
L22           8 S L18,L19,L21
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L23           8 S E21-E28 AND L5
L24             STR L6
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L30          24 S L26
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L32           3 S L29 AND (ZHAO R? OR YONGXIN ? OR CHARI ?)/AU
L33           3 S L29 AND IMMUNOGEN?/PA,CS
L34           3 S L29,L32,L33

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L36          12 S L26
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=> d ide can tot l22

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     (phosphonooxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(3-
     mercapto-1-oxopropyl)amino]- (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C34 H29 Cl N5 O7 P S
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA  CAplus document type:  Patent
RL.P   Roles from patents:  BIOL (Biological study); PREP (Preparation); PRP
       (Properties); USES (Uses)

Absolute stereochemistry.
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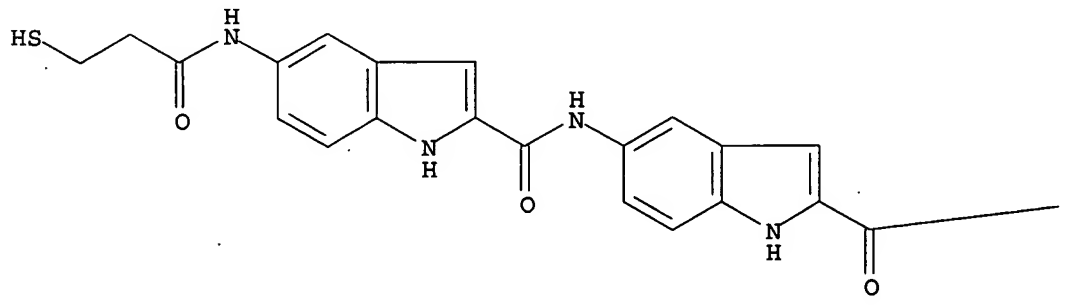
PAGE 1-A



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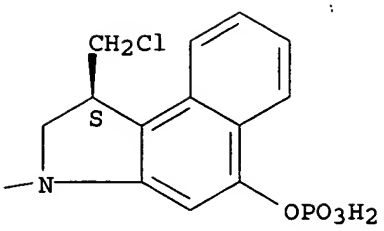

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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

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RN **615538-47-1** REGISTRY
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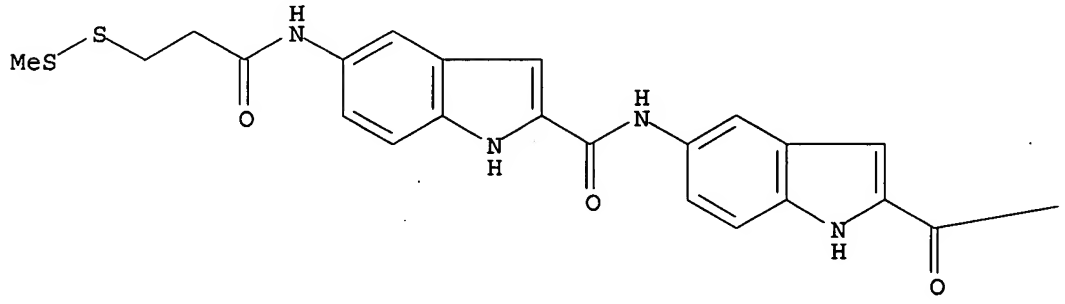
FS STEREOSEARCH
MF **C35 H31 Cl N5 O7 P S2**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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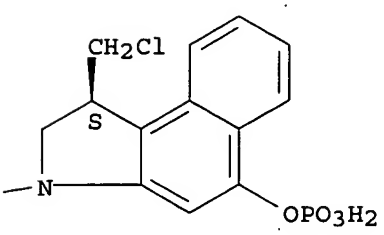

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REFERENCE 1: 139:341741

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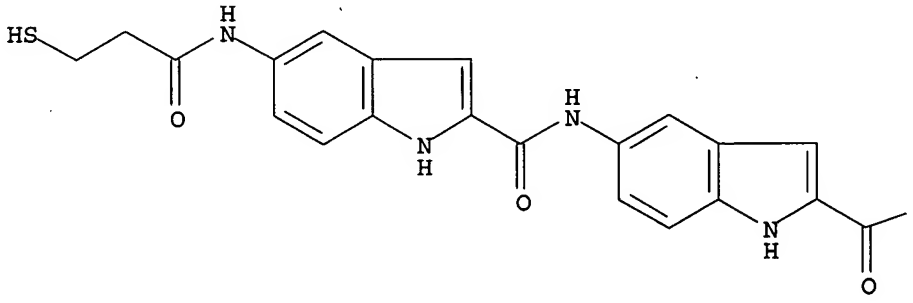
FS STEREOSEARCH
MF C45 H46 Cl N7 O5 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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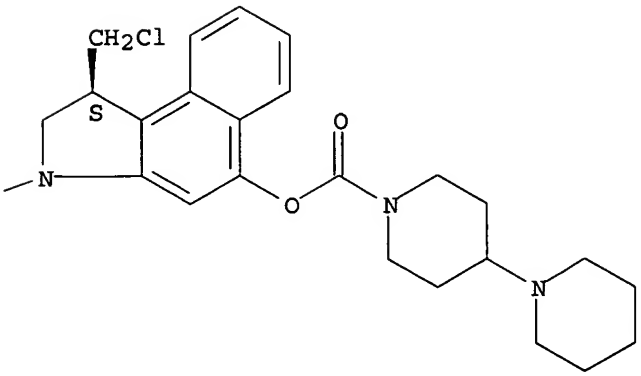

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

L22 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2004 ACS on STN
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MF C46 H48 Cl N7 O5 S2
SR CA
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DT.CA CAplus document type: Patent
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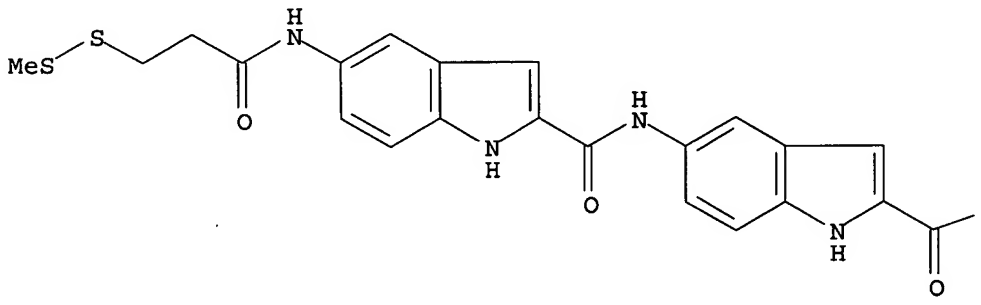
Absolute stereochemistry.

PAGE 1-A



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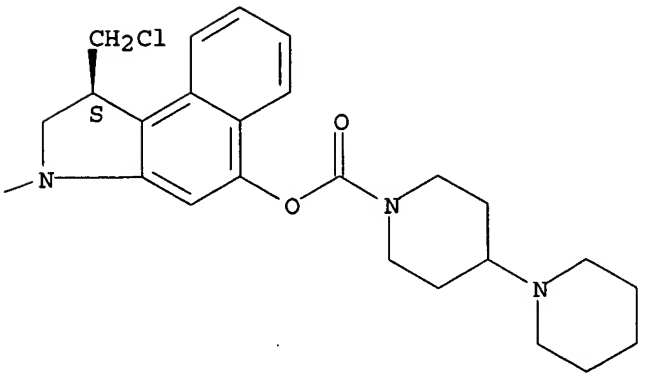

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REFERENCE 1: 139:341741

L22 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2004 ACS on STN
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FS STEREOSEARCH
MF C41 H40 Cl N7 O5 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
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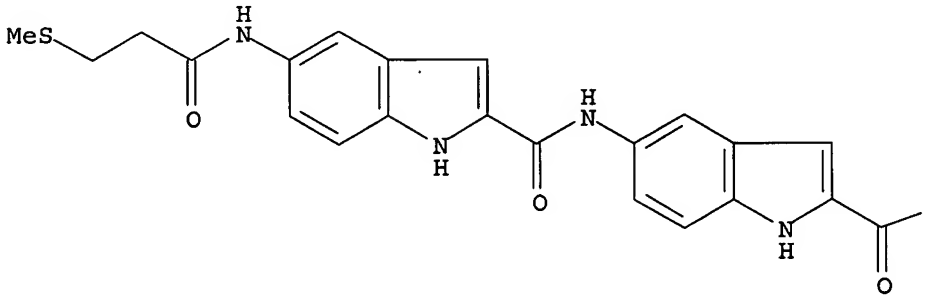
Absolute stereochemistry.

PAGE 1-A



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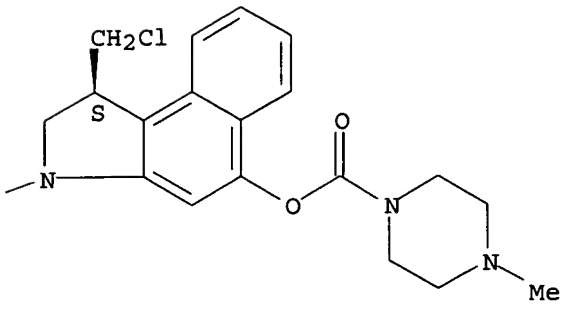

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REFERENCE 1: 139:341741

L22 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2004 ACS on STN
RN **615538-42-6** REGISTRY
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FS STEREOSEARCH

MF C41 H40 Cl N7 O5 S2
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DT.CA CAplus document type: Patent
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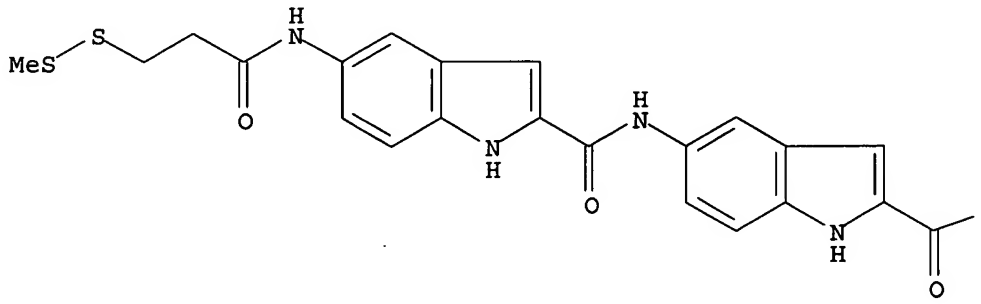
Absolute stereochemistry.

PAGE 1-A



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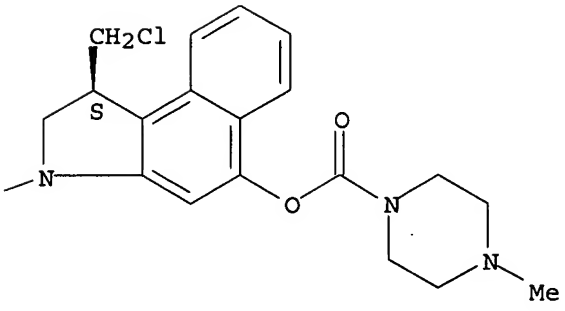

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REFERENCE 1: 139:341741

L22 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2004 ACS on STN
RN **501666-85-9** REGISTRY
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MF **C35 H30 Cl N5 O4 S2**
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DT.CA CAplus document type: Patent
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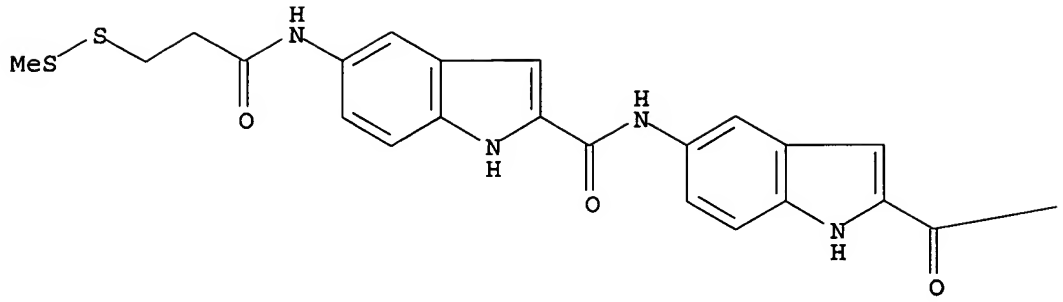
Absolute stereochemistry.

PAGE 1-A



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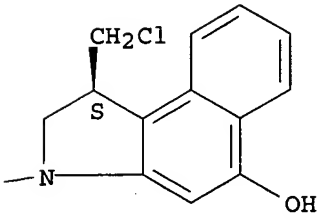

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REFERENCE 1: 139:341741

REFERENCE 2: 138:238007

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MF **C34 H28 Cl N5 O4 S**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Journal
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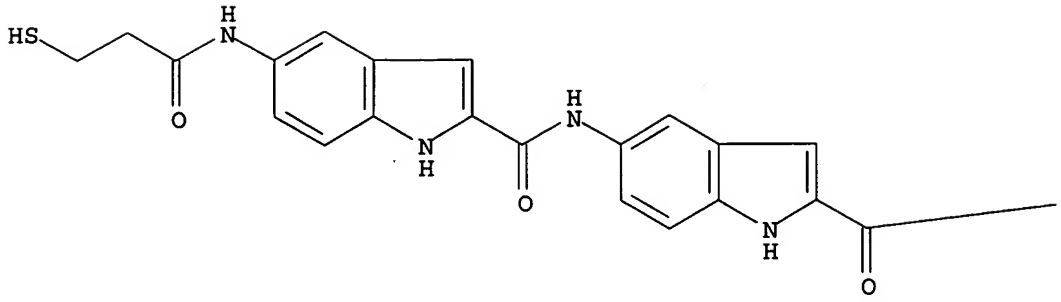
Absolute stereochemistry.

PAGE 1-A



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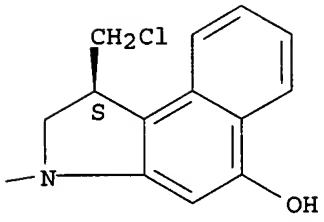

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 123:306084

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 29 Sep 2004 VOL 141 ISS 14
FILE LAST UPDATED: 28 Sep 2004 (20040928/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l34 all hitstr tot

L34 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:836793 HCAPLUS
DN 139:341741
ED Entered STN: 24 Oct 2003
TI Improved prodrugs of CC-1065 analogs
IN **Zhao, Robert Yongxin; Chari, Ravi V. J.**
PA **Immunogen, Inc., USA**
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 26
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003086318	ICM	A61K
US 2003199519	ECLA	A61K031/407; A61K031/4545; A61K031/496; A61K031/675; C07D209/60; C07F009/572V; C07F009/6558B
US 2004109867	ECLA	A61K031/407; C07D209/60; C07F009/572V; C07F009/6558B; A61K031/4545; A61K031/496; A61K031/675

AB Prodrugs of analogs of the antitumor antibiotic CC-1065 are described, comprising both (i) a cleavable protective group, such as a piperazino carbamate, a 4-piperidino-piperidino carbamate or a phosphate, in which the protecting group confers enhanced water solubility and stability upon the prodrug, and (ii) a moiety, such as a disulfide, that can conjugate to a cell binding reagent, e.g., an antibody. The therapeutic use of such prodrug conjugates is also described. These prodrugs of cytotoxic agents have therapeutic use because they can deliver cytotoxic prodrugs to a specific cell population for enzymic conversion to cytotoxic drugs in a targeted fashion.
ST antibiotic CC1065 analog prodrug prepn tumor targeting
IT Antibodies and Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cell binding agents; preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
IT Drug delivery systems
(conjugates of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
IT Antitumor agents
Neoplasm

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT Drug delivery systems
(prodrugs; preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 501441-05-0P **501666-85-9P 615538-42-6P**
615538-45-9P 615538-47-1P 615538-49-3P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT **615538-44-8P 615538-46-0P 615538-48-2P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 92-54-6 4897-50-1, 4-Piperidino-piperidine 7693-46-1, 4-Nitrophenyl chloroformate 10025-87-3, Phosphoric trichloride 17176-77-1, Dibenzylphosphite 51805-45-9, Tris-(2-carboxyethyl) phosphine hydrochloride 138148-59-1 501441-01-6 564476-35-3 615538-50-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 615538-51-7P 615538-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

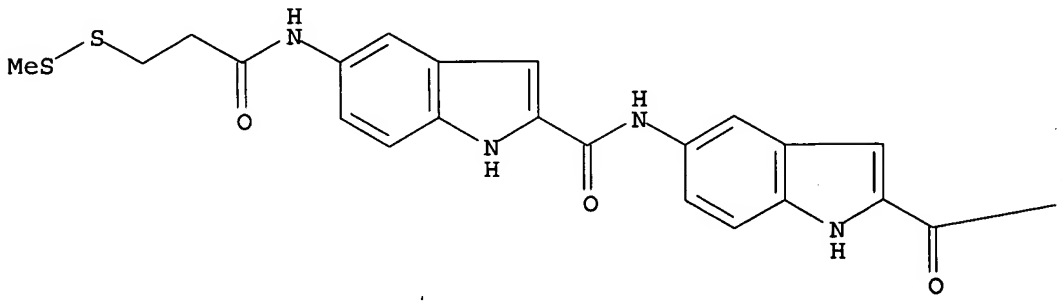
IT 615538-53-9P 615538-54-0P 615538-55-1P 615538-56-2P 615538-57-3DP, salt 615538-58-4P 615538-59-5DP, salt
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT **501666-85-9P 615538-42-6P 615538-45-9P**
615538-47-1P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

RN 501666-85-9 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[[3-(methyldithio)-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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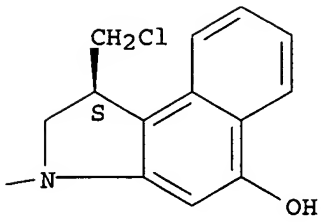
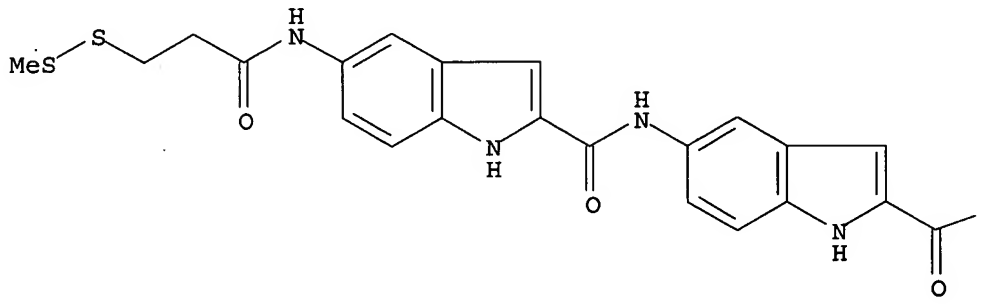


RN 615538-42-6 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-methyl-, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[5-[[[5-[[3-(methyldithio)-1-oxopropyl]amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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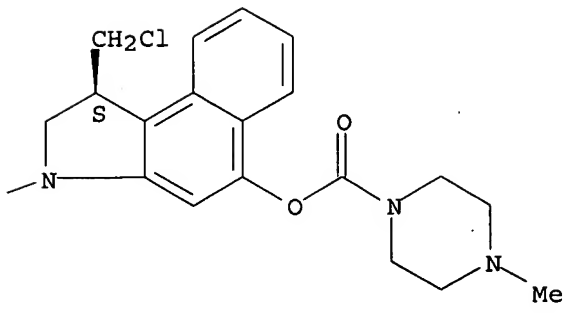
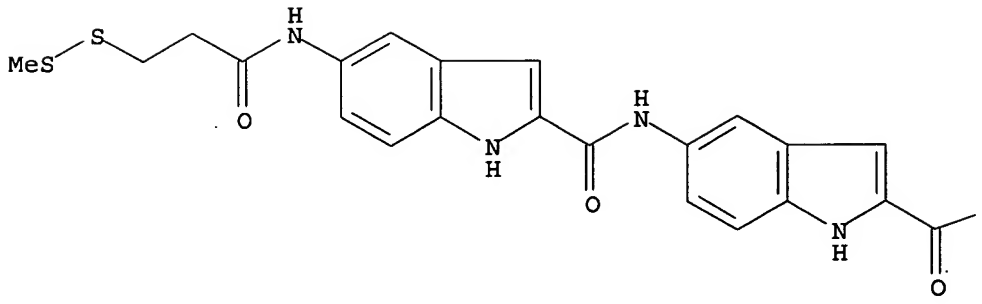


RN 615538-45-9 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[5-[[[5-[[3-(methyldithio)-1-oxopropyl]amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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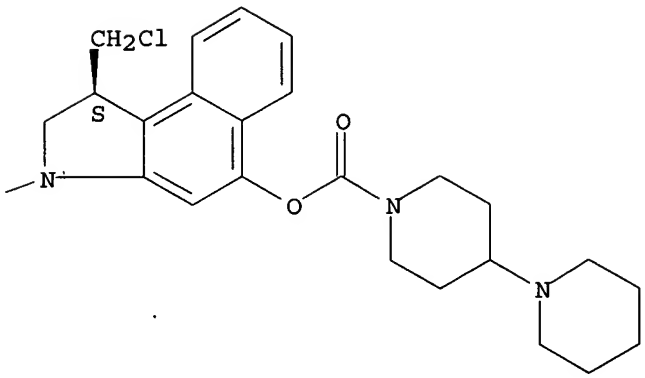

RN 615538-47-1 HCAPLUS
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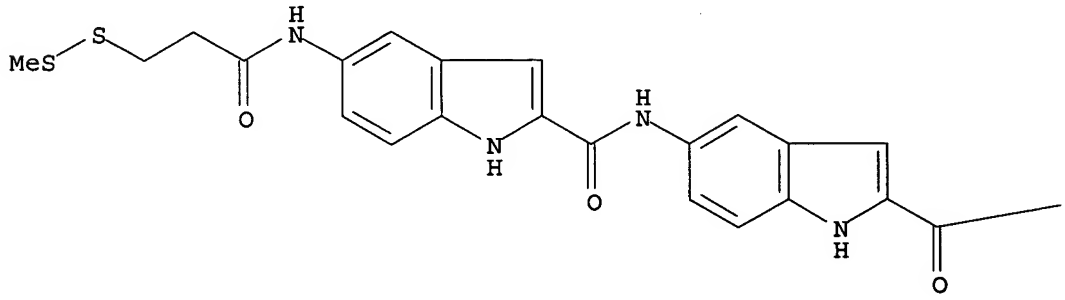
Absolute stereochemistry.

PAGE 1-A



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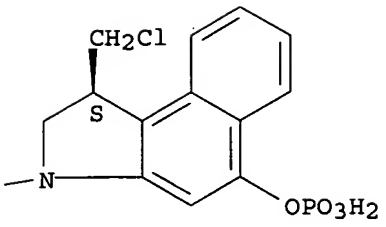


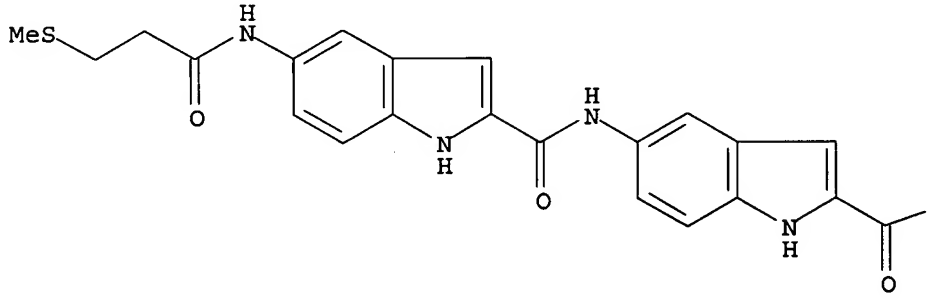
IT **615538-44-8P 615538-46-0P 615538-48-2P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

RN 615538-44-8 HCAPLUS

CN 1-Piperazinecarboxylic acid, 4-methyl-, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[5-[[[5-[[3-(methylthio)-1-oxopropyl]amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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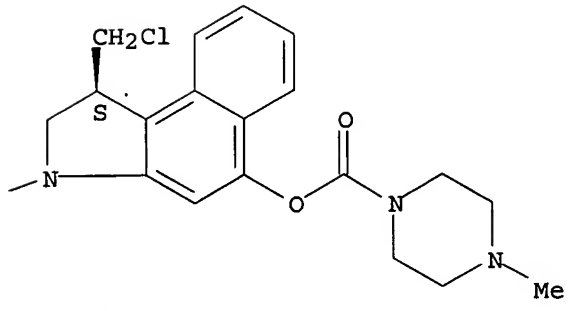
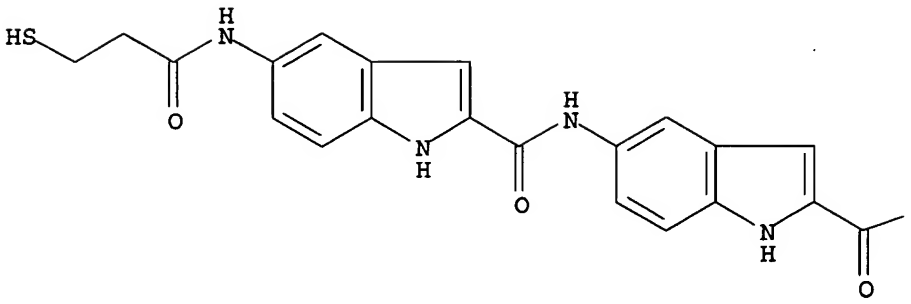


RN 615538-46-0 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[5-[[[5-[(3-mercapto-1-oxopropyl)amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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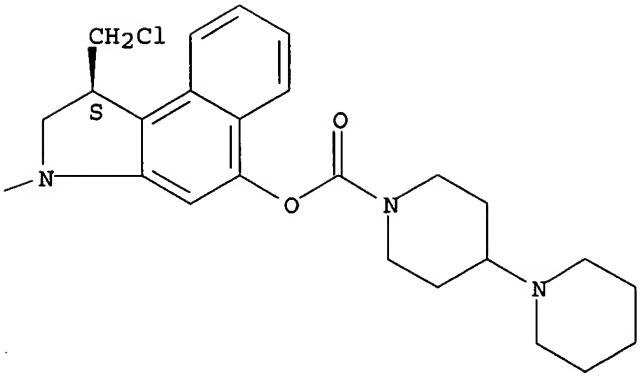
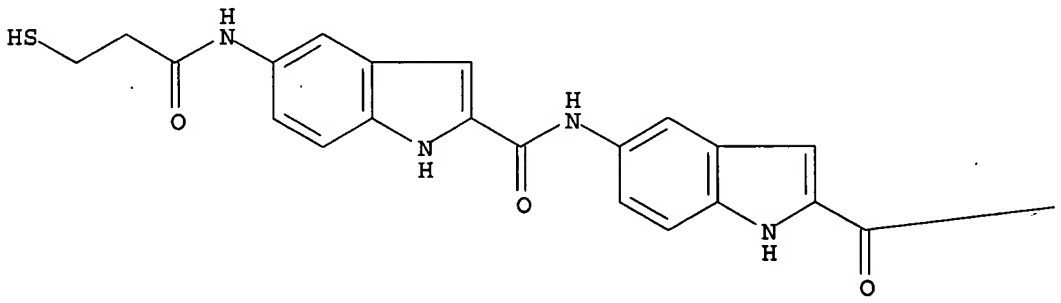


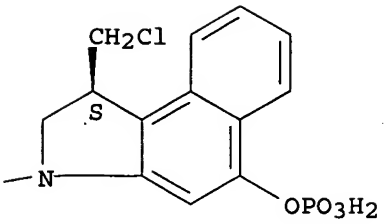
RN 615538-48-2 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-(phosphonooxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(3-mercapto-1-oxopropyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L34 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:217996 HCAPLUS
DN 138:238007
ED Entered STN: 20 Mar 2003
TI Improved synthesis of (-)-5-hydroxy-1(S)-chloromethyl-1,2-dihydro-3H-benz[e]indole, an intermediate in the preparation of CC-1065 analogs
IN **Yongxin, Robert; Chari, Ravi V. J.**
PA **Immunogen, Inc., USA**
SO U.S., 15 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07D209-56
NCL 548450000
CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6534660	B1	20030318	US 2002-116052	20020405
	US 6586618	B1	20030701	US 2002-265329	20021007
	US 2003195365	A1	20031016	US 2002-265452	20021007
	WO 2003087055	A1	20031023	WO 2003-US7276	20030319

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-116052 A3 20020405
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6534660	ICM	C07D209-56
	NCL	548450000
US 2003195365	ECLA	C07D209/60

OS CASREACT 138:238007; MARPAT 138:238007
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed is an improved synthesis of 5-hydroxy-1(S)-chloromethyl-1,2-

dihydro-3H-benz[e]indole [I; seco(-)CBI] comprising (a) protecting the hydroxy and amino groups of 1-hydroxy-3-naphthylamine with the same protecting group, (b) performing halogenation, alkylation, and ring closure reactions to provide the N,O-protected racemate of I, (c) isolating the (-)-isomer, and (d) removing the protecting groups. By using the same protecting group for the amino and hydroxy groups, this method eliminates redundant protection and deprotection steps, shortens synthesis time, improves product yield, and improves separation of enantiomers. Further disclosed is an improved syntheses of a wide variety of CC-1065 analogs that comprise a CBI alkylating moiety, such as the cell-targeted antitumor antibiotic DC1 and its derivs. For example, 1,3-dihydroxynaphthalene was aminated with NH3 and converted to N-(tert-butoxycarbonyl)-1-(tert-butoxycarbonyloxy)-3-naphthylamine (69%) with (BOC)2O in the presence of DIPEA in THF. Iodination with N-iodosuccinimide (86%), alkylation with (Z)-1,3-dichloropropene in the presence of NaH in DMF (93%), and ring closure using Bu3SnH in the presence of AIBN in benzene (94%) gave the racemic N,O-protected benz[e]indole. The racemic mixture was separated using a chiral HPLC column eluting with 20% i-PrOH in hexane. Deprotection with HCl in the presence of Et3SiH in EtOAc gave (-)-I•HCl in 90% purity. Two synthetic routes for conversion of (-)-I•HCl to DC1-SMe (II) are also provided.

ST stereoselective secoCBI prepn hydroxynaphthylamine alkylation cyclization; benzindole intermediate CC1065 analog prepn

IT Alkylation
Cyclization
(preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT Protective groups
(tert-butoxycarbonyl; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 501440-85-3P, 5-(tert-Butoxycarbonyloxy)-3-(tert-butoxycarbonyl)-1-(chloromethyl)-1,2-dihydro-3H-benz[e]indole
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PYP (Physical process); PREP (Preparation); PROC (Process)
(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 501440-87-5P
RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 16730-20-4P, 5-Nitroindole-2-carboxylic acid 71086-99-2P, Ethyl 5-aminoindole-2-carboxylate 152213-42-8P, tert-Butyl 5-nitroindole-2-carboxylate 152213-43-9P, tert-Butyl 5-aminoindole-2-carboxylate 501440-80-8P 501440-82-0P 501440-84-2P, 2-[N-(tert-Butoxycarbonyl)-N-(3-chloro-2-propen-1-yl)amino]-4-(tert-butoxycarbonyloxy)-1-iodonaphthalene 501440-88-6P, tert-Butyl 5-[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-carboxylate 501440-90-0P, tert-Butyl 5-[[(5-aminoindol-2-yl)carbonyl]amino]indole-2-carboxylate 501440-92-2P 501440-94-4P 501440-95-5P 501440-97-7P 501440-99-9P, Ethyl 5-[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-carboxylate 501441-01-6P, 5-[[(5-Nitroindol-2-yl)carbonyl]amino]indole-2-carboxylic acid 501441-05-0P, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 501440-86-4P
RL: BYP (Byproduct); PUR (Purification or recovery); PREP (Preparation)
(preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 132-86-5, 1,3-Dihydroxynaphthalene 542-75-6, 1,3-Dichloropropene

16732-57-3, Ethyl 5-nitroindole-2-carboxylate 24424-99-5, Di-tert-butyl dicarbonate 68617-64-1, 3-(2-Pyridyldithio)propionic acid 138148-59-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 130007-89-5P, 5-Hydroxy-1-(S)-((chloromethyl))-1,2-dihydro-3H-benz[e]indole hydrochloride 299411-68-0P, 5-Hydroxy-1-(S)-((chloromethyl))-1,2-dihydro-3H-benz[e]indole
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(target intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT **501666-85-9P** 501666-87-1P
RL: IMF (Industrial manufacture); PREP (Preparation)
(target product; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Boger, D; Chem Rev 1997, V97, P787 HCAPLUS

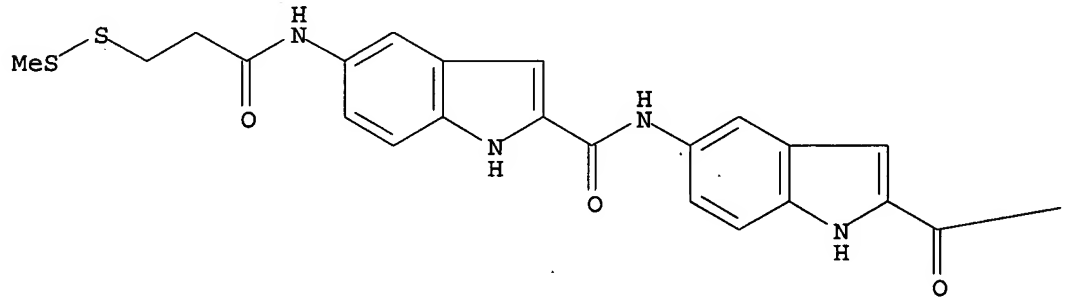
IT **501666-85-9P**
RL: IMF (Industrial manufacture); PREP (Preparation)
(target product; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

RN 501666-85-9 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[[3-(methyldithio)-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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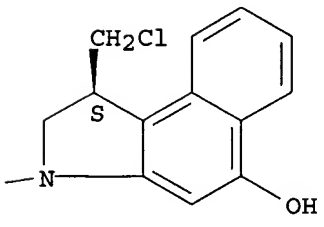


L34 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:809548 HCAPLUS

DN 123:306084

ED Entered STN: 23 Sep 1995

TI Enhancement of the selectivity and antitumor efficacy of a CC-1065 analog

through immunoconjugate formation

AU **Chari, Ravi V. J.**; Jackel, Kristine A.; Bourret, Lizabeth A.; Derr, Susan M.; Tadayoni, B. Mitra; Mattocks, Kristin M.; Shah, Sudhir A.; Liu, Changnian; Blattler, Walter A.; Goldmacher, Victor S.

CS **ImmunoGen. Inc., Cambridge, MA, 02139-4239, USA**

SO Cancer Research (1995), 55(18), 4079-84
CODEN: CNREA8; ISSN: 0008-5472

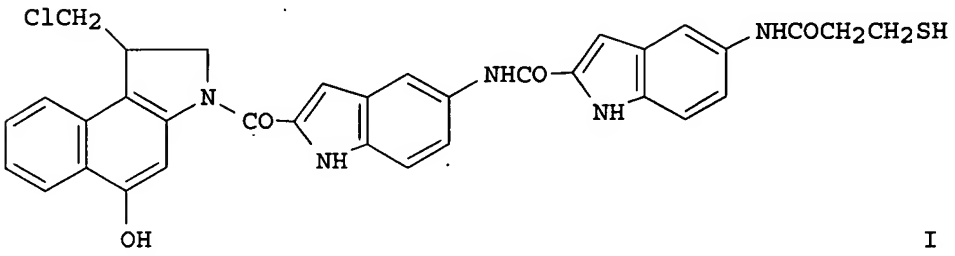
PB American Association for Cancer Research

DT Journal

LA English

CC 1-6 (Pharmacology)
Section cross-reference(s): 63

GI



I

AB Bis-indolyl-(seco)-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one compds. are synthetic analogs of CC-1065 that are highly cytotoxic toward a broad spectrum of tumor cell lines. One of these compds., called DC1 (I), was conjugated to antibodies via novel cleavable disulfide linkers. Conjugates of DC1 with murine mAbs anti-B4 and N901 directed against tumor-associated antigens CD19 and CD56, resp., proved to be extremely potent and antigen selective in killing target cells in culture. DC1 conjugates with humanized versions of anti-B4 and N901 antibodies were also constructed and demonstrated to be as cytotoxic and selective as the resp. murine antibody conjugates. The anti-B4-DC1 conjugate showed antitumor efficacy in an aggressive metastatic human B-cell lymphoma survival model in SCID mice and completely cured animals bearing large tumors. Anti-B4-DC1 was considerably more effective in this tumor model than doxorubicin, cyclophosphamide, etoposide, or vincristine at their maximum tolerated doses.

ST metastasis inhibitor immunoconjugate CC1065 analog; antitumor indolylcyclopropabenzindolone deriv immunoconjugate

IT Antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(CD19, tumor-associated; enhancement of selectivity and antitumor efficacy of CC-1065 analog through immunoconjugate formation)

IT Antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(CD56, tumor-associated; enhancement of selectivity and antitumor efficacy of CC-1065 analog through immunoconjugate formation)

IT Pharmaceutical dosage forms
(immunoconjugates, enhancement of selectivity and antitumor efficacy of CC-1065 analog through immunoconjugate formation)

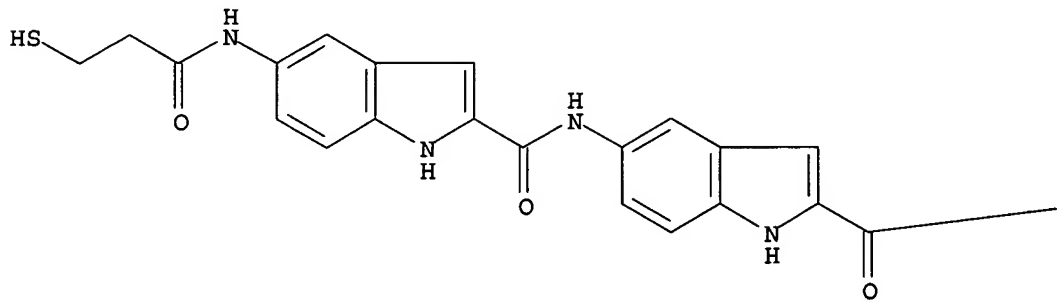
IT Neoplasm inhibitors
(metastasis, enhancement of selectivity and antitumor efficacy of CC-1065 analog through immunoconjugate formation)

IT **169901-27-3D**, conjugates with murine mAbs anti-B4 and N901
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancement of selectivity and antitumor efficacy of CC-1065 analog

through immunoconjugate formation)
IT **169901-27-3D**, conjugates with murine mAbs anti-B4 and N901
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancement of selectivity and antitumor efficacy of CC-1065 analog through immunoconjugate formation)
RN 169901-27-3 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(3-mercapto-1-oxopropyl)amino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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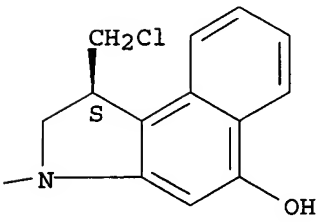

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L31 ANSWER 1 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:836793 HCAPLUS
DN 139:341741
ED Entered STN: 24 Oct 2003
TI Improved prodrugs of CC-1065 analogs
IN Zhao, Robert Yongxin; Chari, Ravi V. J.
PA Immunogen, Inc., USA
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 26

1 structure displayed per reference. See pages 85-end for all hits

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003086318	A2	20031023	WO 2003-US7282	20030320 <--
	WO 2003086318	A3	20040325		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,
MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG

US 2003199519 A1 20031023 US 2002-116053 20020405 <--
US 6756397 B2 20040629
US 2004109867 A1 20040610 US 2003-692856 20031027 <--
PRAI US 2002-116053 A 20020405 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003086318	ICM	A61K
US 2003199519	ECLA	A61K031/407; A61K031/4545; A61K031/496; A61K031/675; C07D209/60; C07F009/572V; C07F009/6558B <--
US 2004109867	ECLA	A61K031/407; C07D209/60; C07F009/572V; C07F009/6558B; A61K031/4545; A61K031/496; A61K031/675 <--

AB Prodrugs of analogs of the antitumor antibiotic CC-1065 are described, comprising both (i) a cleavable protective group, such as a piperazino carbamate, a 4-piperidino-piperidino carbamate or a phosphate, in which the protecting group confers enhanced water solubility and stability upon the prodrug, and (ii) a moiety, such as a disulfide, that can conjugate to a cell binding reagent, e.g., an antibody. The therapeutic use of such prodrug conjugates is also described. These prodrugs of cytotoxic agents have therapeutic use because they can deliver cytotoxic prodrugs to a specific cell population for enzymic conversion to cytotoxic drugs in a targeted fashion.

ST antibiotic CC1065 analog prodrug prepn tumor targeting

IT Antibodies and Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cell binding agents; preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT Drug delivery systems
(conjugates of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT Antitumor agents
Neoplasm
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT Drug delivery systems
(prodrugs; preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT **501441-05-0P** 501666-85-9P 615538-42-6P 615538-45-9P
615538-47-1P **615538-49-3P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 615538-44-8P 615538-46-0P 615538-48-2P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 92-54-6 4897-50-1, 4-Piperidino-piperidine 7693-46-1, 4-Nitrophenyl chloroformate 10025-87-3, Phosphoric trichloride 17176-77-1, Dibenzylphosphite 51805-45-9, Tris-(2-carboxyethyl) phosphine hydrochloride 138148-59-1 501441-01-6 564476-35-3 615538-50-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT **615538-51-7P 615538-52-8P**

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT **615538-53-9P 615538-54-0P 615538-55-1P**
615538-56-2P 615538-57-3DP, salt **615538-58-4P**
615538-59-5DP, salt
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT **501441-05-0P 615538-49-3P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT **615538-51-7P 615538-52-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT **615538-53-9P 615538-54-0P 615538-55-1P**
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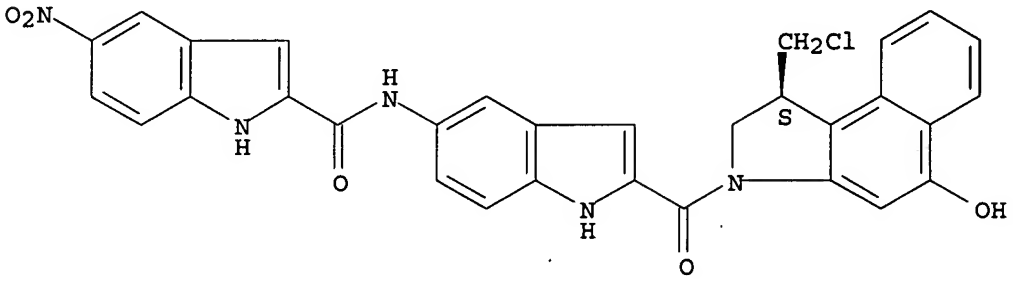
615538-59-5DP, salt
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT **501441-05-0P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

RN 501441-05-0 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:221652 HCAPLUS
DN 138:255007
ED Entered STN: 21 Mar 2003
TI Preparation of CBI analogues of CC 1065 and the duocarmycins for therapeutic use as anticancer agents
IN Boger, Dale L.
PA The Scripps Research Institute, USA
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English

IC ICM C07D
CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003022806	A2	20030320	WO 2002-US28749	20020909 <--
WO 2003022806	A3	20031113		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1423110	A2	20040602	EP 2002-798201	20020909 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRAI US 2001-318179P	P	20010907 <--	
WO 2002-US28749	W	20020909	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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OS MARPAT 138:255007
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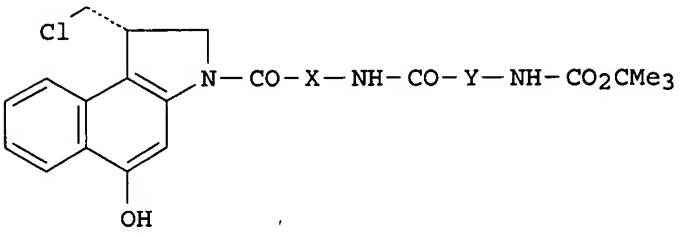

I

AB 132 CBI analogs I [X, Y = arylene, heteroarylene] of CC 1065 and the duocarmycins having dimeric monocyclic, bicyclic, and tricyclic heteroaroms. substituents were synthesized by a parallel route. The resultant analogs were evaluated with respect to their catalytic and cytotoxic activities. The relative contribution of the various dimeric monocyclic, bicyclic, and tricyclic heteroaroms. substituents within the DNA binding domain were characterized. Several of the resultant CBI analogs of CC 1065 and the duocarmycins were characterized as having enhanced catalytic and cytotoxic activities and were identified as having utility as anti-cancer agents. Thus, I (X = Y = -4-C6H4-) was prepared starting from 4-H2NC6H4CO2H and the hydrochloride salt of seco-CBI.

ST duocarmycin analog library prepn antitumor agent; CC1065 analog library prepn antitumor agent

IT DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(alkylation; synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT Alkylating agents, biological
Antitumor agents
Combinatorial library
Human
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT Neoplasm
(treatment; synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT 69866-21-3DP, CC 1065, analogs 118292-34-5DP, Duocarmycin A, analogs 128300-14-1DP, (+)-CBI-CDPI, analogs 130288-24-3DP, (+)-Duocarmycin SA, analogs 166104-33-2DP, (+)-CBI-CDPBI, analogs 166104-36-5DP, (+)-CBI-CDPBO, analogs 372953-14-5P 372953-15-6P 372953-16-7P
372953-17-8P 372953-18-9P 372953-19-0P 372953-20-3P 372953-21-4P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT 99-05-8, 3-Aminobenzoic acid 150-13-0, 4-Aminobenzoic acid 40283-41-8, 2-Amino-4-thiazolecarboxylic acid 42933-44-8 45776-13-4 55341-87-2, 3-Amino-2-thiophenecarboxylic acid 82221-08-7 98589-46-9
130007-89-5, Seco-CBI hydrochloride 152213-40-6 263710-28-7
372953-12-3 372953-13-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT 120506-51-6P 126092-98-6P 138730-83-3P 180258-47-3P 292070-82-7P
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT **372954-24-0P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT **372954-24-0P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

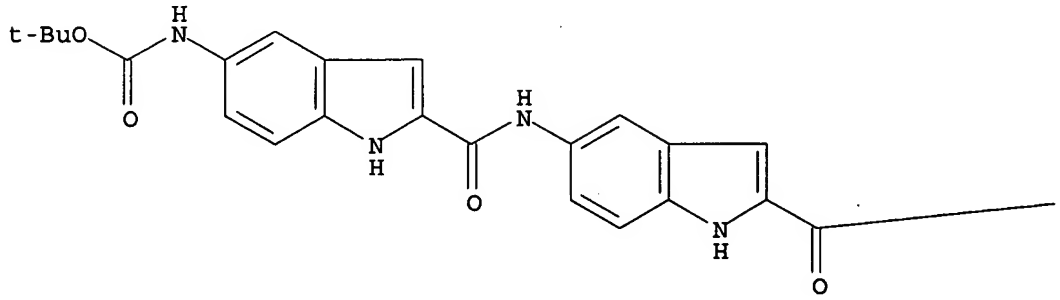
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

RN 372954-24-0 HCAPLUS

CN Carbamic acid, [2-[[[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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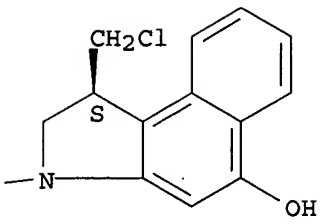

L31 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:217996 HCAPLUS
DN 138:238007
ED Entered STN: 20 Mar 2003
TI Improved synthesis of (-)-5-hydroxy-1(S)-chloromethyl-1,2-dihydro-3H-benz[e]indole, an intermediate in the preparation of CC-1065 analogs
IN Yongxin, Robert; Chari, Ravi V. J.
PA Immunogen, Inc., USA
SO U.S., 15 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07D209-56
NCL 548450000
CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6534660	B1	20030318	US 2002-116052	20020405 <--
US 6586618	B1	20030701	US 2002-265329	20021007 <--
US 2003195365	A1	20031016	US 2002-265452	20021007 <--
WO 2003087055	A1	20031023	WO 2003-US7276	20030319 <--

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PRAI US 2002-116052 A3 20020405 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6534660	ICM	C07D209-56
	NCL	548450000
US 2003195365	ECLA	C07D209/60 <--

OS CASREACT 138:238007; MARPAT 138:238007
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed is an improved synthesis of 5-hydroxy-1(S)-chloromethyl-1,2-

dihydro-3H-benz[e]indole [I; seco(-)CBI] comprising (a) protecting the hydroxy and amino groups of 1-hydroxy-3-naphthylamine with the same protecting group, (b) performing halogenation, alkylation, and ring closure reactions to provide the N,O-protected racemate of I, (c) isolating the (-)-isomer, and (d) removing the protecting groups. By using the same protecting group for the amino and hydroxy groups, this method eliminates redundant protection and deprotection steps, shortens synthesis time, improves product yield, and improves separation of enantiomers. Further disclosed is an improved syntheses of a wide variety of CC-1065 analogs that comprise a CBI alkylating moiety, such as the cell-targeted antitumor antibiotic DC1 and its derivs. For example, 1,3-dihydroxynaphthalene was aminated with NH3 and converted to N-(tert-butoxycarbonyl)-1-(tert-butoxycarbonyloxy)-3-naphthylamine (69%) with (BOC)2O in the presence of DIPEA in THF. Iodination with N-iodosuccinimide (86%), alkylation with (Z)-1,3-dichloropropene in the presence of NaH in DMF (93%), and ring closure using Bu3SnH in the presence of AIBN in benzene (94%) gave the racemic N,O-protected benz[e]indole. The racemic mixture was separated using a chiral HPLC column eluting with 20% i-PrOH in hexane. Deprotection with HCl in the presence of Et3SiH in EtOAc gave (-)-I•HCl in 90% purity. Two synthetic routes for conversion of (-)-I•HCl to DC1-SMe (II) are also provided.

ST stereoselective secoCBI prepn hydroxynaphthylamine alkylation cyclization; benzindole intermediate CC1065 analog prepn

IT Alkylation
Cyclization
(preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT Protective groups
(tert-butoxycarbonyl; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 501440-85-3P, 5-(tert-Butoxycarbonyloxy)-3-(tert-butoxycarbonyl)-1-(chloromethyl)-1,2-dihydro-3H-benz[e]indole
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PYP (Physical process); PREP (Preparation); PROC (Process)
(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

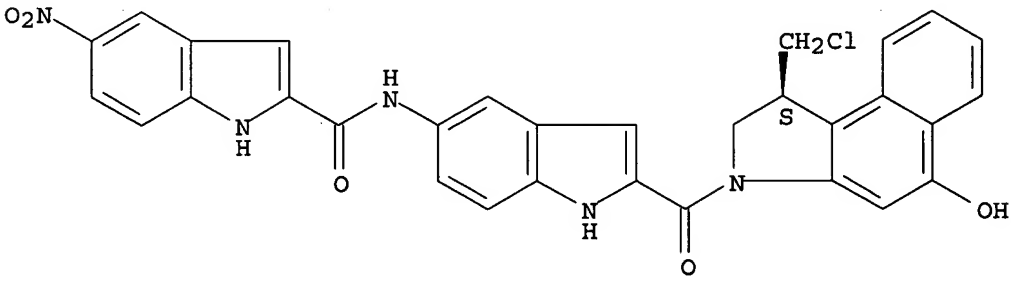
IT 501440-87-5P
RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 16730-20-4P, 5-Nitroindole-2-carboxylic acid 71086-99-2P, Ethyl 5-aminoindole-2-carboxylate 152213-42-8P, tert-Butyl 5-nitroindole-2-carboxylate 152213-43-9P, tert-Butyl 5-aminoindole-2-carboxylate 501440-80-8P 501440-82-0P 501440-84-2P, 2-[N-(tert-Butoxycarbonyl)-N-(3-chloro-2-propen-1-yl)amino]-4-(tert-butoxycarbonyloxy)-1-iodonaphthalene 501440-88-6P, tert-Butyl 5-[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-carboxylate 501440-90-0P, tert-Butyl 5-[[(5-aminoindol-2-yl)carbonyl]amino]indole-2-carboxylate 501440-92-2P 501440-94-4P 501440-95-5P 501440-97-7P 501440-99-9P, Ethyl 5-[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-carboxylate 501441-01-6P, 5-[[(5-Nitroindol-2-yl)carbonyl]amino]indole-2-carboxylic acid **501441-05-0P**, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 501440-86-4P
RL: BYP (Byproduct); PUR (Purification or recovery); PREP (Preparation)
(preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

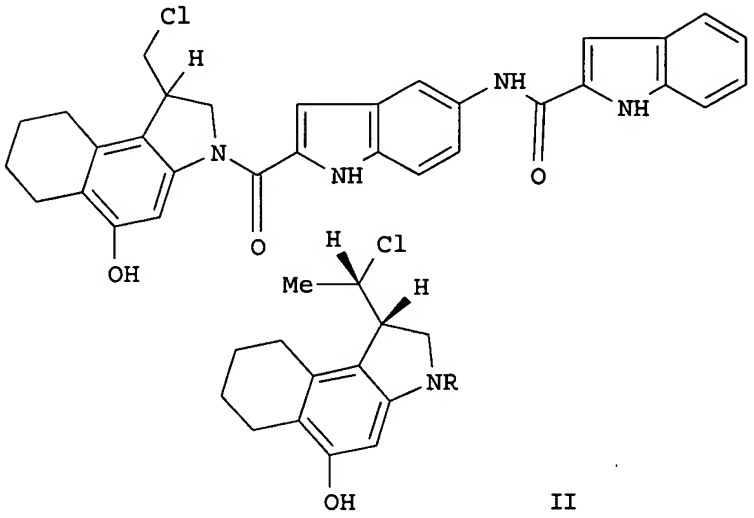
IT 132-86-5, 1,3-Dihydroxynaphthalene 542-75-6, 1,3-Dichloropropene 16732-57-3, Ethyl 5-nitroindole-2-carboxylate 24424-99-5, Di-tert-butyl dicarbonate 68617-64-1, 3-(2-Pyridyldithio)propionic acid 138148-59-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)
IT 130007-89-5P, 5-Hydroxy-1-(S)-((chloromethyl))-1,2-dihydro-3H-benz[e]indole hydrochloride 299411-68-0P, 5-Hydroxy-1-(S)-((chloromethyl))-1,2-dihydro-3H-benz[e]indole
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(target intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)
IT 501666-85-9P **501666-87-1P**
RL: IMF (Industrial manufacture); PREP (Preparation)
(target product; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Boger, D; Chem Rev 1997, V97, P787 HCAPLUS
IT **501441-05-0P**, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)
IT **501666-87-1P**
RL: IMF (Industrial manufacture); PREP (Preparation)
(target product; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)
IT **501441-05-0P**, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)
RN 501441-05-0 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:394360 HCAPLUS
DN 137:201172
ED Entered STN: 28 May 2002
TI Synthesis and biological evaluation of novel analogues and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy
AU Tietze, Lutz F.; Herzig, Tobias; Feuerstein, Tim; Schuberth, Ingrid

CS Georg-August-Universitat Gottingen, Institut fur Organische Chemie, Gottingen, 37077, Germany
SO European Journal of Organic Chemistry (2002), (10), 1634-1645
CODEN: EJOCFK; ISSN: 1434-193X
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1
OS CASREACT 137:201172
GI



I II

AB This paper describes novel seco-analogs, e.g. I, of the cytotoxic antibiotic CC-1065 and their galactoside prodrugs for antibody-directed enzyme prodrug therapy (ADEPT). A partially hydrogenated seco-CCI-analog and the corresponding methyl-CCI analogs were synthesized by alkylation reactions followed by radical cyclization and deprotection. Treatment of the above compds. with the galactose trichloroacetimidate and the bisindolyl-carboxylic acid in the presence of EDC followed by solvolysis gave the desired galactoside prodrugs. In vitro tests showed a strong cytotoxicity for I and a fairly low toxicities for other prepared compds. The selectivity of the galactoside prodrugs was not sufficient for ADEPT. Interestingly, II (R = COOCMe3) did not undergo Winstein cyclization to produce the spirocyclopropylcyclohexadienone moiety.
ST CC1065 seco analog prepn; alkylation radical cyclization CC1065 analog prepn; antibody directed enzyme prodrug therapy galactoside CC1065
IT Chemotherapy
(antibody-directed enzyme; synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)
IT Structure-activity relationship
(antitumor; synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)
IT Bronchi, neoplasm
(carcinoma; synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)
IT Cyclization
(radical; synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and

antibody-directed enzyme prodrug therapy)
IT Alkylation
Antitumor agents
Human
Neoplasm
(synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)
IT **452921-65-2P 452921-66-3P 452921-75-4P**
452921-76-5P 452921-77-6P 452921-78-7P
452921-79-8P 452921-80-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)
IT 119-64-2 542-75-6 926-57-8 86520-63-0 101134-91-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)
IT 50536-99-7P 51522-30-6P 452921-67-4P 452921-68-5P 452921-69-6P
452921-70-9P 452921-71-0P 452921-72-1P 452921-73-2P 452921-74-3P
452921-82-3P 452921-83-4P 452921-84-5P 452921-85-6P 452921-86-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)
IT 69866-21-3DP, CC 1065, analogs 452921-81-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Baird, R; J Am Chem Soc 1963, V85, P567 HCAPLUS
(2) Bieg, T; Synthesis 1985, P76 HCAPLUS
(3) Boger, D; Acc Chem Res 1999, V32, P1043 HCAPLUS
(4) Boger, D; Angew Chem 1996, V108, P1542
(5) Boger, D; Angew Chem Int Ed Engl 1996, V35, P1438 HCAPLUS
(6) Boger, D; Chem Rev 1997, V97, P787 HCAPLUS
(7) Boger, D; Synthesis 1999, P1505 HCAPLUS
(8) Boger, D; Tetrahedron Lett 1998, V39, P2227
(9) Dubowchik, G; Pharmacology & Therapeutics 1999, V83, P67 HCAPLUS
(10) Patel, V; J Org Chem 1997, V62, P8868 HCAPLUS
(11) Schroeter, G; Justus Liebigs Ann Chem 1922, V426, P1 HCAPLUS
(12) Springer, C; Adv Drug Deliv Rev 1997, V26, P151
(13) Syrigos, K; Anticancer Res 1999, V19, P605 HCAPLUS
(14) Tannock, I; Cancer Res 1989, V49, P4373 MEDLINE
(15) Tietze, L; Angem Chem 1996, V108, P2840
(16) Tietze, L; Angew Chem 1990, V102, P812 HCAPLUS
(17) Tietze, L; Angew Chem Int Ed Engl 1990, V29, P782
(18) Tietze, L; Angew Chem Int Ed Engl 1996, V35, P2674 HCAPLUS
(19) Tietze, L; Bioorg Med Chem 2001, V9, P1929 HCAPLUS
(20) Tietze, L; Cancer Res 1989, V49, P4179 HCAPLUS
(21) Tietze, L; ChemBioChem 2001, V2, P758 HCAPLUS
(22) Tietze, L; Molecular Aspects of Chemotherapy 1990
(23) Wirth, H; Justus Liebigs Ann Chem 1960, V643, P84
(24) Zimmermann, P; J Carbohy Chem 1988, V7, P435 HCAPLUS
IT **452921-65-2P 452921-66-3P 452921-75-4P**
452921-76-5P 452921-77-6P 452921-78-7P
452921-79-8P 452921-80-1P

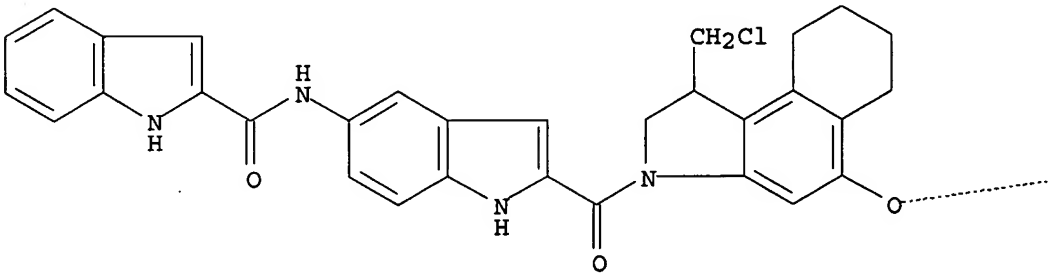
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)

IT **452921-65-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)

RN 452921-65-2 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-5-(β-D-galactopyranosyloxy)-1,2,6,7,8,9-hexahydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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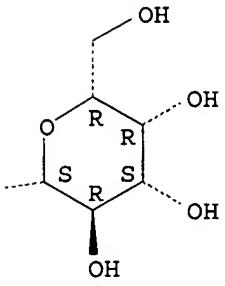

L31 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:816635 HCAPLUS
DN 135:344672
ED Entered STN: 09 Nov 2001
TI Preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy
IN Tietze, Lutz F.; Fecher, Anja; Herzig, Tobias
PA Germany
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM C07D209-00
CC 33-3 (Carbohydrates)
Section cross-reference(s): 1, 27, 63
FAN.CNT 2
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 2001083448	A2	20011108	WO 2001-EP4904	20010502 <--
	WO 2001083448	A3	20020620		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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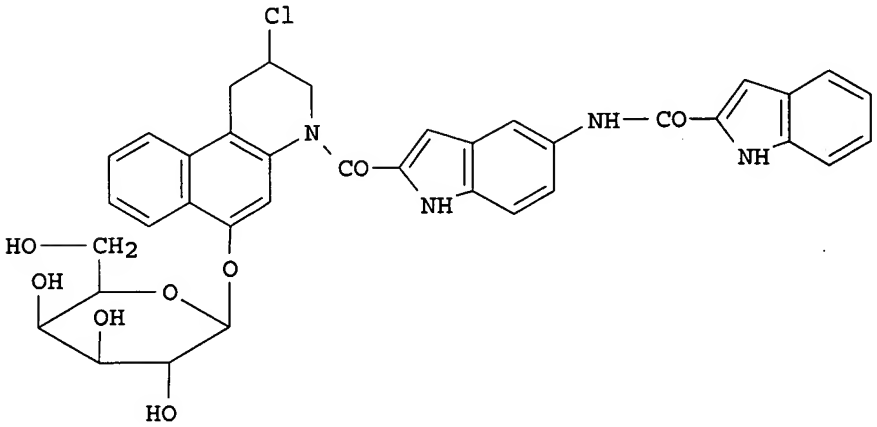
PRAI	DE 2000-10021335	A	20000502 <--		
	DE 2000-10025329	A	20000523 <--		
	WO 2001-EP4904	W	20010502 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001083448	ICM	C07D209-00
US 2004033962	ECLA	C07D209/60; C07D487/04; C07H017/02 <--

OS MARPAT 135:344672

GI



I

AB To improve the selectivity of cytostatics used for cancer therapy, novel prodrugs of 6-hydroxy-2,3-dihydro-1H-indoles, 5-hydroxy-1,2-dihydro-3H-pyrrolo[3,2-e]indoles and 5-hydroxy-1,2-dihydro-3H-benzo[e]indoles as well as of 6-hydroxy-1,2,3,4-tetrahydro-benzo[f]-quinolines have been developed which can be used in ADEP therapy (antibody directed enzyme prodrug therapy). The novel prodrugs are characterized by a marked difference in toxicity between the prodrug and the drug on which it is based and by a very high effectiveness of the drug. The high selectivity of the novel prodrugs is probably due to the fact that they contain, unlike the prodrugs of a similar kind produced so far, a secondary halide. Thus, (I) was synthesized by reaction of N-Boc-protected (4H)-2-O-(tert-butyldiphenylsilyl)hydroxy-6-(phenylmethoxy) benzo[f]quinoline (preparation given) with 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl

trichloroacetimidate, N-deprotection and reaction with 5[((1H-indol-2'-yl)carbonyl)amino]-1H-indol-2-carboxylic acid, desilylation and chlorination, and sugar O-deacetylation. In in vitro tests with human bronchial carcinoma cell line A549, I showed high activity in the presence of added β-D-galactosidase, but little activity alone, showing that it was an effective prodrug.

ST indole cyclization benzoquinoline galactopyranoside prepn anticancer prodrug cytotoxicity chemotherapy; drug delivery system benzoquinoline galactopyranoside prepn; antibody directed enzyme prodrug therapy benzoquinoline galactopyranoside prepn

IT Chemotherapy
(antibody-directed enzyme; preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

IT Antitumor agents
Chemotherapy
Cyclization
Cytotoxicity
Drug delivery systems
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

IT Glycosides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

IT **330206-90-1P** 371155-16-7P 371155-19-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

IT 926-57-8 86520-63-0 101134-91-2 161646-53-3 191732-57-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

IT 330206-88-7P **330206-89-8P** 371155-10-1P 371155-11-2P 371155-12-3P 371155-13-4P 371155-14-5P 371155-15-6P 371155-17-8P 371155-18-9P 371155-20-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

IT **330206-90-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

IT **330206-89-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

IT **330206-90-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

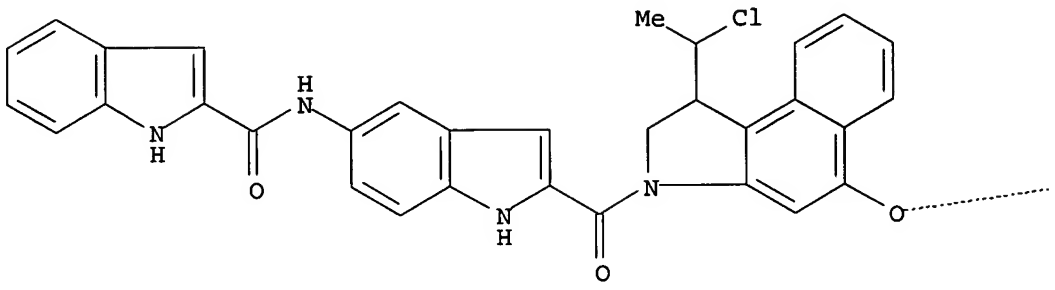
RN 330206-90-1 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[1-(1-chloroethyl)-5-(β-D-

galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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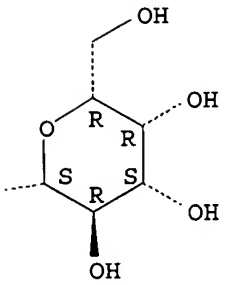


L31 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:752449 HCAPLUS
DN 136:112208
ED Entered STN: 16 Oct 2001
TI Highly selective glycosylated prodrugs of cytostatic CC-1065 analogues for antibody-directed enzyme tumor therapy
AU Tietze, Lutz F.; Herzig, Tobias; Fecher, Anja; Haunert, Frank; Schuberth, Ingrid
CS Inst. fur Organische Chemie, Georg-August-Univ., Gottingen, 37077, Germany
SO ChemBioChem (**2001**), 2(10), 758-765
CODEN: CBCHFX; ISSN: 1439-4227
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
CC 1-3 (Pharmacology)
OS CASREACT 136:112208
AB Novel prodrugs of the cytotoxic antibiotic CC-1065 for an antibody-directed enzyme prodrug therapy (ADEPT) were prepared that show an excellent selectivity with a high toxicity of the corresponding drug. In particular, the seco-CBI analog of CC-1065, 1-chloromethyl-5-hydroxy-1,2-dihydro-3H-benz(e)indole, as well as the novel methyl-seco-CBl analog 1-(1'-chloroethyl)-5-hydroxy-1,2-dihydro-3H-benz[e]indole, were synthesized and transformed into their galactosides 10a and 10b, resp. These galactosides can be cleaved with β-D-galactosidase to give the free cytotoxic compds. They were tested in vitro cytotoxicity assays by using human bronchial carcinoma cells of line A549 in the presence and in the absence of β-D-galactosidase. While the seco-CBI prodrugs revealed only modest selectivity, prodrugs of the methyl-seco-CBi analog bearing an anti orientation of the substituents at the two stereogenic centers of the N-heterocycle displayed an excellent selectivity with an

ED50 quotient of about 750. The cytotoxicity of the corresponding phenol was rather high, with an ED50 of 1.3 nM. The diastereomer with a syn orientation at the stereogenic centers was much less toxic.

ST glycosylated prodrug CC 1065 analog; antibody directed enzyme tumor therapy CC1065 analog

IT Diastereomers
(CC-1065 analogs; highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)

IT Chemotherapy
(antibody-directed enzyme; highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)

IT Cytotoxicity
Human
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)

IT Drug delivery systems
(prodrugs; highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)

IT **390362-62-6P 390362-63-7P 390362-64-8P**
390362-68-2P 390362-69-3P 390362-70-6P
390362-71-7P 390362-72-8P 390362-73-9P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)

IT 69866-21-3DP, CC-1065, analogs
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)

IT 542-75-6 926-57-8 25952-53-8, N-Ethyl-N'-(3-dimethylaminopropyl)carbodiimide hydrochloride 86520-63-0 90016-93-6 101134-91-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)

IT 122745-40-8P 227084-59-5P 330206-87-6P 330206-88-7P 390362-66-0P 390362-67-1P 390362-74-0P 390362-75-1P 697263-39-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)

IT 122745-41-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)

IT 9031-11-2, β-Galactosidase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Boger, D; Acc Chem Res 1999, V32, P1043 HCAPLUS
(2) Boger, D; Angew Chem 1996, V108, P1542
(3) Boger, D; Angew Chem Int Ed Engl 1996, V35, P1438 HCAPLUS
(4) Boger, D; Chem Rev 1997, V97, P787 HCAPLUS
(5) Boger, D; J Am Chem Soc 1990, V112, P8961 HCAPLUS
(6) Boger, D; Tetrahedron 1991, V47, P2661 HCAPLUS
(7) Boger, D; Tetrahedron Lett 1998, V39, P2227
(8) Chari, R; Cancer Res 1995, V55, P4079 HCAPLUS
(9) Dubowchik, G; Pharmacol Ther 1999, V83, P67 HCAPLUS

(10) Li, L; Cancer Res 1992, V52, P4904 HCAPLUS
(11) Patel, V; J Org Chem 1997, V62, P8868 HCAPLUS
(12) Springer, C; Adv Drug Delivery Rev 1997, V26, P151
(13) Syrigos, K; Anticancer Res 1999, V19, P605 HCAPLUS
(14) Tannock, I; Cancer Res 1989, V49, P4373 MEDLINE
(15) Tietze, L; Angew Chem 1990, V102, P812 HCAPLUS
(16) Tietze, L; Angew Chem 1996, V108, P2840
(17) Tietze, L; Angew Chem Int Ed Engl 1990, V29, P782
(18) Tietze, L; Angew Chem Int Ed Engl 1996, V35, P2674 HCAPLUS
(19) Tietze, L; Cancer Res 1989, V49, P4179 HCAPLUS
(20) Zimmermann, P; J Carbohydr Chem 1988, V7, P435 HCAPLUS

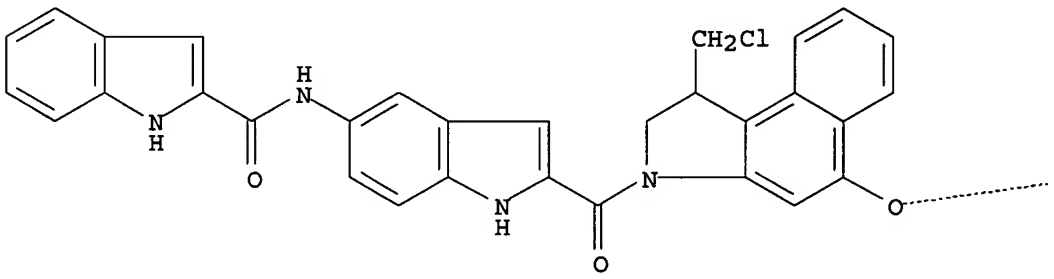
IT **390362-62-6P 390362-63-7P 390362-64-8P**
390362-68-2P 390362-69-3P 390362-70-6P
390362-71-7P 390362-72-8P 390362-73-9P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)

IT **390362-62-6P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)

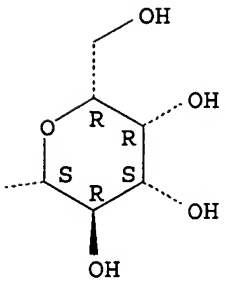
RN 390362-62-6 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-5-(β-D-galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L31 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:667407 HCAPLUS
DN 135:357786

ED Entered STN: 13 Sep 2001
TI Parallel Synthesis and Evaluation of 132 (+)-1,2,9,9a-Tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) Analogues of CC-1065 and the Duocarmycins Defining the Contribution of the DNA-Binding Domain
AU Boger, Dale L.; Schmitt, Harald W.; Fink, Brian E.; Hedrick, Michael P.
CS Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Journal of Organic Chemistry (**2001**), 66(20), 6654-6661
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 9
OS CASREACT 135:357786
AB The solution-phase, parallel synthesis and evaluation of a library of 132 (+)-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) analogs of CC-1065 and the duocarmycins containing dimeric monocyclic, bicyclic, and tricyclic heteroarom. replacements for the DNA-binding domain are described. This systematic study revealed clear trends in the structural requirements for observation of potent cytotoxic activity and DNA alkylation efficiency, the range of which spans a magnitude of ≥10 000-fold. Combined with related studies, these results highlight that the role of the DNA-binding domain goes beyond simply providing DNA-binding selectivity and affinity (10-100-fold enhancement in properties), consistent with the proposal that it contributes significantly to catalysis of the DNA alkylation reaction accounting for as much as an addnl. 1000-fold enhancement in properties.
ST tetrahydrochloromethylbenzindolone library prepn soln phase; CC1065 duocarmycin analog library cytotoxicity; DNA alkylation binding domain tetrahydrochloromethylbenzindolone library
IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(binding domain; synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)
IT Alkylating agents, biological
Combinatorial library
Cytotoxicity
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)
IT 128300-14-1 130007-93-1 **135306-53-5** 166104-33-2
166104-36-5
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)
IT 372953-14-5P 372953-15-6P 372953-16-7P 372953-17-8P 372953-18-9P
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372953-75-8P 372953-76-9P 372953-77-0P 372953-78-1P 372953-79-2P
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372954-41-1P 372954-42-2P 372954-43-3P 372954-44-4P 372954-45-5P
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RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT 99-05-8, 3-Aminobenzoic acid 150-13-0, 4-Aminobenzoic acid 40283-41-8, 2-Amino-4-thiazolecarboxylic acid 42933-44-8 45776-13-4 82221-08-7 89499-38-7 98589-46-9 130007-89-5 152213-40-6 263710-28-7 372953-12-3 372953-13-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Ambrose, C; J Mol Biol 1989, V210, P255 HCAPLUS
(2) Amishiro, N; Chem Pharm Bull 1999, V47, P1393 HCAPLUS
(3) Asai, A; J Am Chem Soc 1994, V116, P4171 HCAPLUS
(4) Atwell, G; J Med Chem 1999, V42, P3400 HCAPLUS
(5) Baraldi, P; J Med Chem 2001, V44, P2536 HCAPLUS
(6) Boger, D; Acc Chem Res 1999, V32, P1043 HCAPLUS
(7) Boger, D; Angew Chem, Int Ed Engl 1996, V35, P1438 HCAPLUS
(8) Boger, D; Bioorg Med Chem 1994, V2, P115 HCAPLUS
(9) Boger, D; Bioorg Med Chem 1995, V3, P1429 HCAPLUS
(10) Boger, D; Bioorg Med Chem 1995, V3, P761 HCAPLUS
(11) Boger, D; Bioorg Med Chem 1997, V5, P233 HCAPLUS
(12) Boger, D; Bioorg Med Chem 1997, V5, P263 HCAPLUS
(13) Boger, D; Bioorg Med Chem Lett 2001, V11, P2021 HCAPLUS
(14) Boger, D; Chem Rev 1997, V97, P787 HCAPLUS
(15) Boger, D; Chem-Biol Interact 1990, V73, P29 MEDLINE
(16) Boger, D; Chemtracts:Org Chem 1991, V4, P329 HCAPLUS
(17) Boger, D; J Am Chem Soc 1989, V111, P6461 HCAPLUS
(18) Boger, D; J Am Chem Soc 1990, V112, P4623 HCAPLUS
(19) Boger, D; J Am Chem Soc 1990, V112, P8961 HCAPLUS
(20) Boger, D; J Am Chem Soc 1991, V113, P6645 HCAPLUS
(21) Boger, D; J Am Chem Soc 1992, V114, P5487 HCAPLUS
(22) Boger, D; J Am Chem Soc 1993, V115, P9872 HCAPLUS
(23) Boger, D; J Am Chem Soc 1994, V116, P1635 HCAPLUS
(24) Boger, D; J Am Chem Soc 1994, V116, P7996 HCAPLUS
(25) Boger, D; J Am Chem Soc 1997, V119, P4977 HCAPLUS
(26) Boger, D; J Am Chem Soc 1997, V119, P4987 HCAPLUS
(27) Boger, D; J Am Chem Soc 2000, V122, P6325 HCAPLUS
(28) Boger, D; J Am Chem Soc 2000, V122, P6382 HCAPLUS
(29) Boger, D; J Am Chem Soc, in press
(30) Boger, D; J Org Chem 1990, V55, P4499 HCAPLUS
(31) Boger, D; J Org Chem 1990, V55, P5823 HCAPLUS
(32) Boger, D; J Org Chem 1992, V57, P2873 HCAPLUS

(33) Boger, D; J Org Chem 1995, V60, P1271 HCAPLUS
(34) Boger, D; J Org Chem 2000, V65, P4088 HCAPLUS
(35) Boger, D; Proc Natl Acad Sci U S A 1995, V92, P3642 HCAPLUS
(36) Boger, D; Synlett 1997, P515 HCAPLUS
(37) Boger, D; Synthesis 1999, P1505 HCAPLUS
(38) Boger, D; Tetrahedron 1991, V47, P2661 HCAPLUS
(39) Boger, D; Tetrahedron Lett 1990, V31, P793 HCAPLUS
(40) Boger, D; Tetrahedron Lett 1998, V39, P2227
(41) Chang, A; J Am Chem Soc 2000, V122, P4856 HCAPLUS
(42) Eis, P; J Mol Biol 1997, V272, P237 HCAPLUS
(43) Fregeau, N; J Am Chem Soc 1995, V117, P8917 HCAPLUS
(44) Hanka, L; J Antibiot 1978, V31, P1211 HCAPLUS
(45) Hurley, L; Biochemistry 1988, V27, P3886 HCAPLUS
(46) Hurley, L; Chem Res Toxicol 1988, V1, P315
(47) Hurley, L; J Am Chem Soc 1990, V112, P4633 HCAPLUS
(48) Hurley, L; Science 1984, V226, P843 HCAPLUS
(49) Iida, H; Recent Res Dev Synth Org Chem 1998, V1, P17 HCAPLUS
(50) Jia, G; Chem Commun 1999, P119 HCAPLUS
(51) Jia, G; Heterocycl Commun 1998, V4, P557 HCAPLUS
(52) Johnson, D; Supramolecular Chemistry 1996, V4, P73 HCAPLUS
(53) Schnell, J; J Am Chem Soc 1999, V121, P5645 HCAPLUS
(54) Smith, J; J Mol Biol 2000, V300, P1195 HCAPLUS
(55) Tao, Z; Angew Chem, Int Ed 1999, V38, P650 HCAPLUS
(56) Tao, Z; J Am Chem Soc 1999, V121, P4961 HCAPLUS
(57) Tao, Z; J Am Chem Soc 1999, V121, P4961 HCAPLUS
(58) Tao, Z; J Am Chem Soc 2000, V122, P1602 HCAPLUS
(59) Wang, Y; Anti-Cancer Drug Des 1996, V11, P15 HCAPLUS
(60) Wang, Y; Heterocycles 1993, V36, P1399 HCAPLUS
(61) Warpehoski, M; Advances in DNA Sequence Specific Agents 1992, V1, P217 HCAPLUS

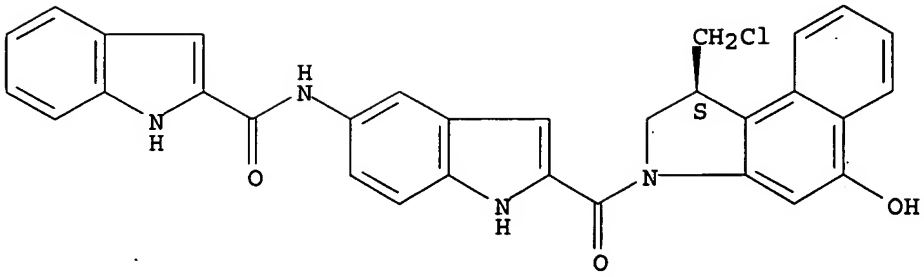
IT **135306-53-5**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT **372954-24-0P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT **135306-53-5**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

RN 135306-53-5 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L31 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:224194 HCAPLUS
DN 134:237751
ED Entered STN: 29 Mar 2001
TI Synthesis of glycosidic prodrugs containing 6-Hydroxy-2,3-dihydro-1H-indolene, 5-Hydroxy-1,2-dihydro-3H-pyrrolo[3,2-e]indolene or 5-Hydroxy-1,2-dihydro-3H-benzo[e]indolene for use in cancer therapy
IN Tietze, Lutz F.; Herzig, Tobias
PA Germany
SO Ger. Offen., 26 pp.
CODEN: GWXXBX
DT Patent
LA German
IC ICM C07H017-08
ICS C07D209-10; C07D487-02; A61K031-40
CC 33-3 (Carbohydrates)
Section cross-reference(s): 1, 27, 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	WO 2001083448	A2	20011108	WO 2001-EP4904	20010502 <--
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	DE 2000-10025329	A	20000523 <--		
	WO 2001-EP4904	W	20010502 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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US 2004033962	ECLA	C07D209/60; C07D487/04; C07H017/02 <--

OS MARPAT 134:237751
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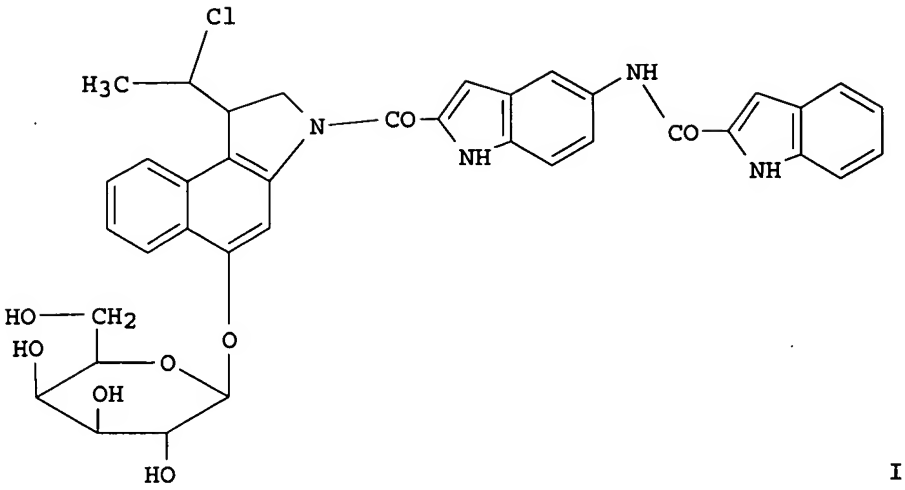


I

AB Title compds. (e.g. I) were prepared as prodrugs for use in the treatment of cancer by the antibody directed enzymic prodrug therapy (ADEPT) method, and were characterized by a high toxicity difference between prodrug and underlying drug and a very high effectiveness of the drug being delivered. Thus, 2-amino-4-benzyloxy-N-((H3C)3COC(O))-1-iodonaphthalene was reacted with an E/Z mixture of 1,3-dichlorobut-2-ene, and the product cyclized to give 5-benzyloxy-3-((H3C)3COC(O))-1-(1'-chloroethyl)-1,2-dihydro-3H-benzo[e]indole, which was O-deprotected and reacted with o-(2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl)-trichloroacetimidate and 5-[((1H-indol-2'-yl)carbonyl)amino]-1H-indol-2-carboxylic acid to give the tetra-O-acetylated I, was was then O-deprotected to give I. In antiproliferative in vivo tests using cell line A 549 cells, I had ED50 2 nM, when incubated with β-D-galactosidase vs. ED50 1470 nM without added enzyme.

ST indolene glycoside cyclization prepn prodrug cancer therapy

IT Antitumor agents
Cyclization
(preparation of glycosidic prodrugs containing substituted indolenes for use in
cancer therapy)

IT Glycosides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of glycosidic prodrugs containing substituted indolenes for use in
cancer therapy)

IT Drug delivery systems
(prodrugs; preparation of glycosidic prodrugs containing substituted indolenes
for use in cancer therapy)

IT **330206-90-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of glycosidic prodrugs containing substituted indolenes for use in
cancer therapy)

IT 7415-31-8 10075-38-4 86520-63-0 101134-91-2 161646-53-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of glycosidic prodrugs containing substituted indolenes for use in
cancer therapy)

IT 330206-86-5P 330206-87-6P 330206-88-7P **330206-89-8P**
330206-91-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of glycosidic prodrugs containing substituted indolenes for use in
cancer therapy)

IT **330206-90-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of glycosidic prodrugs containing substituted indolenes for use in
cancer therapy)

IT **330206-89-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of glycosidic prodrugs containing substituted indolenes for use in
cancer therapy)

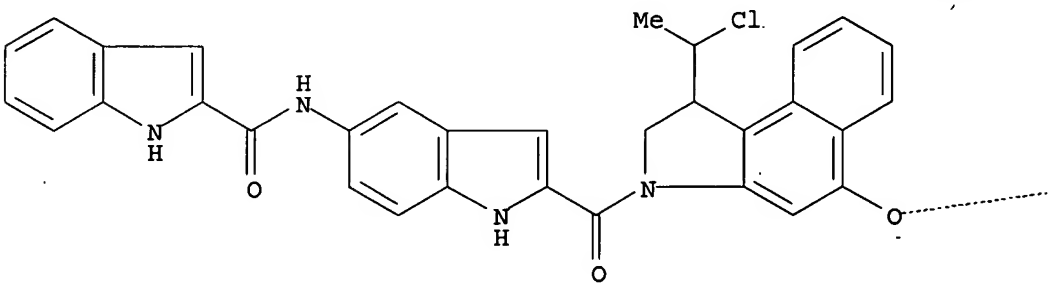
IT **330206-90-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of glycosidic prodrugs containing substituted indolenes for use in
cancer therapy)

RN 330206-90-1 HCAPLUS

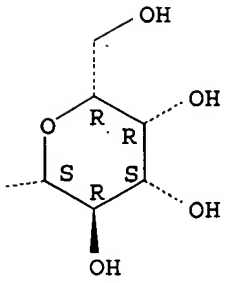
CN 1H-Indole-2-carboxamide, N-[2-[[1-(1-chloroethyl)-5-(β-D-galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

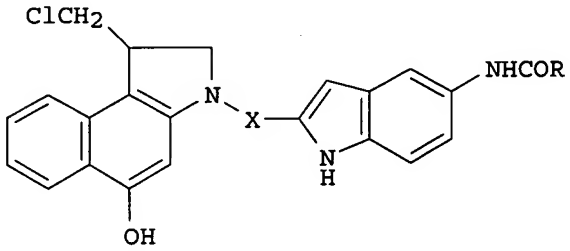


PAGE 1-B



L31 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:173482 HCAPLUS
DN 132:321743
ED Entered STN: 17 Mar 2000
TI Synthesis and Preliminary Biological Evaluations of CC-1065 Analogues: Effects of Different Linkers and Terminal Amides on Biological Activity
AU Wang, Yuqiang; Yuan, Huiling; Ye, Wenqing; Wright, Susan C.; Wang, Hong; Larrick, James W.
CS Panorama Research Inc., Mountain View, CA, 94043, USA
SO Journal of Medicinal Chemistry (2000), 43(8), 1541-1549
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1
GI



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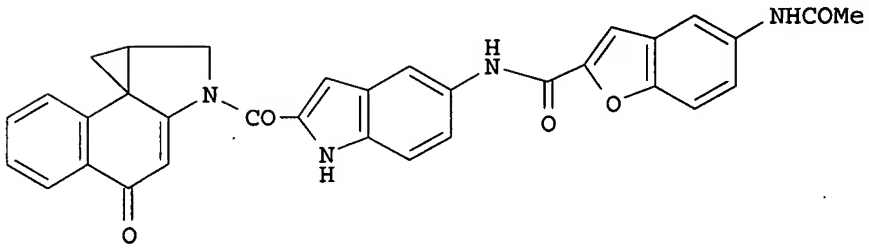


III

AB CC-1065 analogs possessing a biol. active CBI functional group and amide-substituted indole and benzofuran were synthesized. The IC50 values of compds. (I) (R = 5-acetamino-1H-indol-2-yl; X = CO) (II), bearing two indoles, and I (R = Me; X =CO), bearing only one indole, are 0.4 and 3 nM, resp., against U937 leukemia cells in vitro. The IC50 values of compds. I (R = 5-butyramino-1H-benzofuran-2-yl; X = CO), bearing a butyramino group, and I (R = 5-acetamino-1H-benzofuran-2-yl; X = CO), bearing an acetamino group, are 0.008 and 0.4 nM, resp., against U937 leukemia cells in vitro. I (R = 5-acetamino-1H-indol-2-yl; X = CO-CH=CH), bearing a double-bond linker, is about 4-fold more potent than I (R = Me; X = CO), bearing no double-bond linker. II is highly potent against all cell lines tested in the NCI in vitro screening with IC50 values in the 0.1-5 nM range for most cell lines. II and III are highly active against L1210 leukemia in mice. II is also active against B16BL6 melanoma in mice. Most importantly, II and III are not myelosuppressive at therapeutically EDs. The mechanism of tumor cell death is through induction of apoptosis, and is accompanied by DNA fragmentation.

ST CC 1065 analog prepn; antileukemic activity cytotoxicity CC 1065 analog; antitumor antibiotic benzofuran indole linker terminal amide effect

IT Antitumor agents
Antitumor agents
(antibiotic; preparation, effects of different linkers and terminal amides on antitumor activity of CC-1065 analogs)

IT Antibiotics
Antibiotics
(antitumor; preparation, effects of different linkers and terminal amides on antitumor activity of CC-1065 analogs)

IT Antitumor agents
(leukemia; preparation, effects of different linkers and terminal amides on antitumor activity of CC-1065 analogs)

IT Cytotoxicity
(of CC-1065 analogs)

IT 69866-21-3P, (+)-CC 1065
RL: PNU (Preparation, unclassified); PREP (Preparation)
(effects of different linkers and terminal amides on biol. activity of CC-1065 analogs)

IT 199806-51-4P 266349-02-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antitumor activity of CC-1065 analogs)

IT 199806-32-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and cytotoxicity of CC-1065 analogs)

IT 199806-34-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation, DNA fragmentation and cytotoxicity of CC-1065 analogs)

IT **199806-33-2P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, cytotoxicity and hematol. effects of CC-1065 analogs)

IT 106-31-0, Butanoic anhydride 2605-67-6 122745-46-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation, effects of different linkers and terminal amides on biol. activity of CC-1065 analogs)

IT 199806-35-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, effects of different linkers and terminal amides on biol. activity of CC-1065 analogs)

IT 10242-12-3 16732-57-3 104862-11-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation, effects of different linkers and terminal amides on biol. activity of CC-1065 analogs)

IT 1646-30-6P 110887-42-8P 199805-80-6P 199805-81-7P 199805-82-8P 199805-89-5P 199805-93-1P 199805-96-4P 199805-99-7P 199806-02-5P 199806-03-6P 199806-04-7P 199806-10-5P 266348-99-6P 266349-00-2P 266349-01-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, effects of different linkers and terminal amides on biol. activity of CC-1065 analogs)

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD

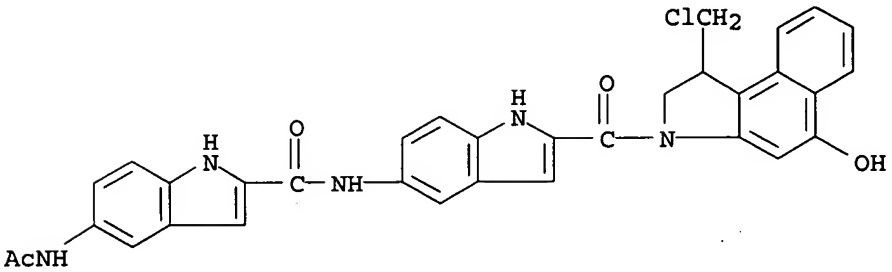
RE
(1) Anon; NCI clinical trials database 1998
(2) Aristoff, P; Adv Med Chem 1993, V2, P67 HCAPLUS
(3) Aristoff, P; J Med Chem 1993, V36, P1956 HCAPLUS
(4) Aristoff, P; J Org Chem 1992, V57, P6234 HCAPLUS
(5) Baraldi, P; Anti-Cancer Drug Des 1997, V12, P555 HCAPLUS
(6) Baraldi, P; Farmaco 1997, V52, P711 HCAPLUS
(7) Baraldi, P; Farmaco 1997, V52, P717 HCAPLUS
(8) Barry, M; Biochem Pharmacol 1990, V40, P2353 HCAPLUS
(9) Bhuyan, B; Cancer Res 1982, V42, P3532 HCAPLUS
(10) Boger, D; Acc Chem Res 1995, V20, P20
(11) Boger, D; Bioorg Med Chem 1995, V3, P1429 HCAPLUS
(12) Boger, D; Bioorg Med Chem 1995, V3, P761 HCAPLUS
(13) Boger, D; Chem Rev 1997, V97, P787 HCAPLUS
(14) Boger, D; J Am Chem Soc 1990, V112, P4623 HCAPLUS
(15) Boger, D; J Am Chem Soc 1992, V114, P9319
(16) Boger, D; J Am Chem Soc 1998, V120, P11554 HCAPLUS
(17) Boger, D; J Org Chem 1989, V54, P1238 HCAPLUS
(18) Boger, D; J Org Chem 1990, V55, P5823 HCAPLUS
(19) Boger, D; J Org Chem 1996, V61, P1710 HCAPLUS
(20) Boger, D; J Org Chem 1996, V61, P4894 HCAPLUS
(21) Boger, D; J Org Chem 1997, V62, P8875 HCAPLUS
(22) Boger, D; J Org Chem 1998, V63, P8004 HCAPLUS
(23) Boger, D; J Org Chem 1999, V64, P5241 HCAPLUS
(24) Boyd, M; Principles Practices Oncol 1989, V3, P1
(25) Chiang, S; Biochemistry 1994, V33, P7033 HCAPLUS
(26) Fregeau, N; J Am Chem Soc 1995, V117, P8917 HCAPLUS
(27) Fukuda, Y; Bioorg Med Chem Lett 1998, V8, P2003 HCAPLUS
(28) Hanka, L; J Antibiot 1978, V31, P1211 HCAPLUS
(29) Hurley, L; J Am Chem Soc 1990, V112, P4633 HCAPLUS
(30) Hurley, L; Science 1984, V226, P843 HCAPLUS
(31) Ichimura, M; J Antibiot 1988, V41, P1205
(32) Kaufmann, S; Cancer Res 1989, V49, P5870 HCAPLUS
(33) Lown, J; US 5502068 1996 HCAPLUS
(34) Martin, D; J Antibiot 1980, V33, P902 HCAPLUS
(35) Martin, D; J Antibiot 1981, V34, P1119 HCAPLUS
(36) McGovren, J; J Antibiot 1984, V37, P63 HCAPLUS
(37) Milbank, J; J Med Chem 1999, V42, P649 HCAPLUS
(38) Ogawa, T; J Antibiot 1989, V42, P1219
(39) Reynolds, V; Biochemistry 1985, V24, P6220
(40) Swenson, D; Cancer Res 1982, V42, P2021
(41) Takahashi, I; J Antibiot 1988, V41, P1915 HCAPLUS
(42) Wang, Y; US 5843937 1998 HCAPLUS
(43) Wang, Y; Anti-Cancer Drug Des 1996, V11, P15 HCAPLUS
(44) Wang, Y; J Med Chem 1993, V36, P4172 HCAPLUS
(45) Warpehoski, M; J Med Chem 1988, V31, P590 HCAPLUS
(46) Wrasidlo, W; Bioorg Med Chem 1994, V4, P631 HCAPLUS
(47) Wright, S; Biochem Biophys Res Commun 1998, V245, P797 HCAPLUS
(48) Wright, S; J Exp Med 1994, V180, P2113 HCAPLUS
(49) Wright, S; J Exp Med 1997, V186, P1107 HCAPLUS
(50) Yasuzawa, T; Chem Pharm Bull 1988, V36, P3720

IT **199806-33-2P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, cytotoxicity and hematol. effects of CC-1065 analogs)

IT **199806-33-2P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, cytotoxicity and hematol. effects of CC-1065 analogs)

RN 199806-33-2 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-(acetylamino)-N-[2-[[1-(chloromethyl)-1,2-

dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



L31 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:550372 HCAPLUS
DN 131:237670
ED Entered STN: 31 Aug 1999
TI CBI prodrug analogs of CC-1065 and the duocarmycins
AU Boger, Dale L.; Boyce, Christopher W.; Garbaccio, Robert M.; Searcey, Mark; Jin, Qing
CS Dep. Chemistry, Skaggs Institute Chemical Biology, La Jolla, CA, 92037, USA
SO Synthesis (**1999**), (Spec. Iss.), 1505-1509
CODEN: SYNTBF; ISSN: 0039-7881
PB Georg Thieme Verlag
DT Journal
LA English
CC 1-6 (Pharmacology)
Section cross-reference(s): 26
AB The preparation of a small series of CBI-indole2 prodrugs is detailed.
ST CC1065 CBI prodrug analog antitumor prepn; duocarmycin CBI prodrug analog antitumor prepn
IT Antitumor agents
(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)
IT Drug delivery systems
(prodrugs; preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)
IT 130288-24-3P, Duocarmycin SA 135306-52-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); BIOL (Biological study); PREP (Preparation)
(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)
IT **135306-53-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)
IT **244154-60-7P 244154-61-8P 244154-62-9P**
244154-63-0P 244154-64-1P 244154-65-2P
244154-68-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)
IT 69866-21-3P, CC-1065

RL: BSU (Biological study, unclassified); PNU (Preparation, unclassified); BIOL (Biological study); PREP (Preparation)
(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)

IT 103-71-9, Phenyl isocyanate, reactions 109-01-3, N-Methylpiperazine 72547-44-5 101134-91-2 130007-86-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)

IT 244154-66-3P 244154-67-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Alberts, S; Clin Cancer Res 1998, V4, P2111 HCAPLUS
(2) Aristoff, P; Advances in Medicinal Chemistry 1993, V2, P67 HCAPLUS
(3) Asai, A; J Am Chem Soc 1994, V116, P4171 HCAPLUS
(4) Boger, D; Acc Chem Res 1995, V28, P20 HCAPLUS
(5) Boger, D; Angew Chem, Int Ed Engl 1996, V35, P1439
(6) Boger, D; Bioorg Med Chem 1995, V3, P1429 HCAPLUS
(7) Boger, D; Bioorg Med Chem Lett 1991, V1, P115 HCAPLUS
(8) Boger, D; Chem Rev 1997, V97, P787 HCAPLUS
(9) Boger, D; Chemtracts: Org Chem 1991, V4, P329 HCAPLUS
(10) Boger, D; J Am Chem Soc 1989, V111, P6461 HCAPLUS
(11) Boger, D; J Org Chem 1990, V55, P5824
(12) Boger, D; J Org Chem 1992, V57, P2873 HCAPLUS
(13) Boger, D; J Org Chem 1995, V60, P1271 HCAPLUS
(14) Boger, D; Proc Natl Acad Sci USA 1995, V92, P3642 HCAPLUS
(15) Houghton, P; Cancer Chemother Pharmacol 1995, V36, P45 HCAPLUS
(16) Hurley, L; Acc Chem Res 1986, V19, P230 HCAPLUS
(17) Hurley, L; Molecular Aspects of Anticancer Drug-DNA Interactions 1993, V1, P89
(18) Li, L; Cancer Res 1992, V52, P4904 HCAPLUS
(19) Nagamura, S; Bioorg Med Chem 1996, V4, P1379 HCAPLUS
(20) Nagamura, S; Bioorg Med Chem Lett 1996, V6, P2147 HCAPLUS
(21) Nagamura, S; Chem Pharm Bull 1995, V43, P1530 HCAPLUS
(22) Nagamura, S; Chem Pharm Bull 1996, V44, P1723 HCAPLUS
(23) Van Tellingen, O; Cancer Res 1998, V58, P2410 HCAPLUS
(24) Warpehoski, M; Advances in DNA Sequence Specific Agents 1992, V1, P217 HCAPLUS
(25) Warpehoski, M; Chem Res Toxicol 1988, V1, P315 HCAPLUS
(26) Warpehoski, M; Molecular Basis of Specificity in Nucleic Acid-Drug Interactions 1990, P531 HCAPLUS
(27) Warpehoski, M; Tetrahedron Lett 1986, V27, P4103 HCAPLUS
(28) Yasuzawa, T; Chem Pharm Bull 1995, V43, P378 HCAPLUS

IT **135306-53-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)

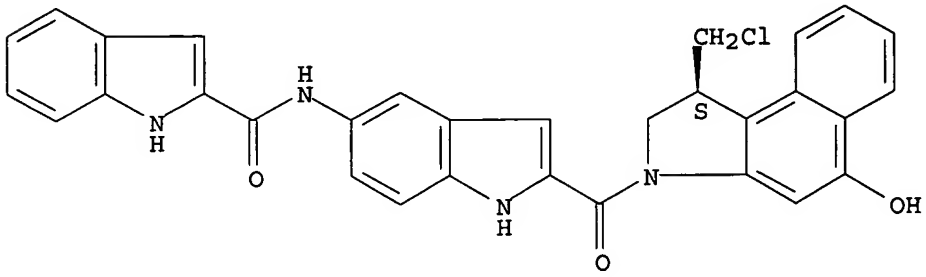
IT **244154-60-7P 244154-61-8P 244154-62-9P 244154-63-0P 244154-64-1P 244154-65-2P 244154-68-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)

IT **135306-53-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)

RN 135306-53-5 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L31 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:805723 HCAPLUS
DN 128:61379
ED Entered STN: 26 Dec 1997
TI Synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins
IN Boger, Dale L.
PA Scripps Research Institute, USA; Boger, Dale L.
SO PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D209-90
ICS C07D403-02; C07D403-14; C07D403-06; C07D417-14
CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9745411	A1	19971204	WO 1997-US9076	19970530 <--
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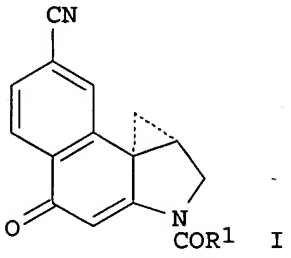
	US 1996-23346P	P	19960912 <--		
	WO 1997-US9076	W	19970530 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9745411	ICM	C07D209-90
	ICS	C07D403-02; C07D403-14; C07D403-06; C07D417-14
US 6060608	ECLA	C07D209/94; C07D209/96; C07D403/06; C07D417/14; C07D487/10 <--

OS MARPAT 128:61379

GI



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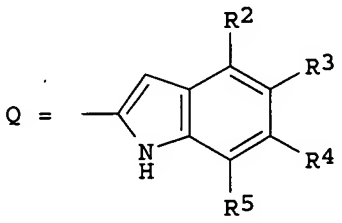
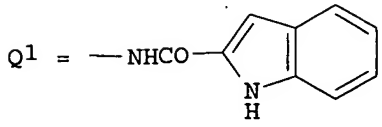
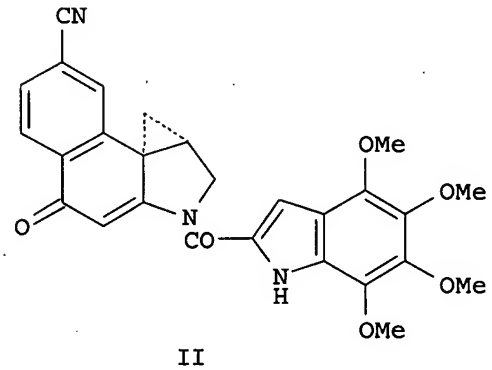






II

AB Analogs of antitumor antibiotics CC-1065 and the duocarmycins I (R1 = C1-C6-alkyl, Q; R2R3 form a pyrrolidine ring containing the vinylene group with the proviso that R4 and R5 = H; R2 = H and R3 = Q1 with the proviso that R4 and R5 = H; R2 = H, R3, R4, R5 = H, MeO) were prepared as compds. which possess systematic and extensive modifications in the DNA binding subunits attached to a 1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) alkylation subunit. The analogs have potent cytotoxic activity and are efficacious antitumor compds. Thus, 3-(tert-butyloxycarbonyl)-1-(chloromethyl)-8-cyano-5-hydroxy-1,2-dihydro-3H-benz[e]indole, prepared in a multistep procedure from m-bromobenzaldehyde and di-Et succinate, was acylated with 5,6,7-trimethoxy-2-indolecarboxylic acid followed by intramol. cyclization to give CCBI-TMI (II). The antitumor IC50(L1210) of II was 7 pM.

ST antitumor CC1055 duocarmycin analog prepn; cyclopropabenzindolone antitumor antibiotic prepn

IT Antitumor agents
(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

IT 176442-53-8P 178963-04-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

IT 178962-98-6P 178962-99-7P 178963-00-3P 178963-01-4P 178963-02-5P
178963-03-6P 181574-83-4P 182957-16-0P 182957-17-1P 182957-18-2P
182957-19-3P 188637-83-4P 188637-86-7P 188637-92-5P 188637-98-1P
188638-21-3P 200352-00-7P 200352-01-8P 200352-02-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

IT 11116-31-7, Bleomycin A2 69866-21-3, (+)-CC 1065 118292-34-5,
(+)-Duocarmycin A 127379-15-1 128300-13-0 130007-87-3 130288-24-3,
(+)-Duocarmycin SA 132746-32-8 144732-53-6 155861-66-8 155861-67-9
155861-68-0 155861-69-1 155861-70-4 157035-51-3 157035-51-3
188638-16-6 188638-17-7 200351-88-8 200351-92-4 200351-94-6
200351-97-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

IT 178877-12-8P 178877-13-9P 178877-14-0P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

IT 106-95-6, Allyl bromide, reactions 123-25-1, Diethyl succinate
870-63-3 1477-50-5, 1H-Indole-2-carboxylic acid 3132-99-8,
3-Bromobenzaldehyde 4382-54-1 4755-77-5 14794-31-1 15026-17-2
16732-73-3 24610-33-1 62209-77-2 77924-28-8 78175-36-7
82692-00-0 101134-91-2 105518-47-6 122745-36-2 128781-07-7
130007-86-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

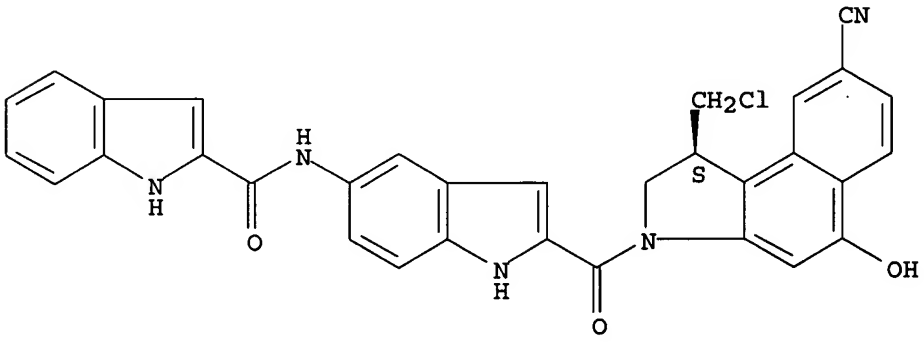
IT 130007-89-5P 178876-98-7P 178877-00-4P 178877-02-6P 178877-03-7P
178877-04-8P 178877-05-9P 178877-06-0P 178877-07-1P 178877-08-2P
178877-09-3P 178877-11-7P 178877-17-3P 178877-18-4P 178877-19-5P
178877-31-1P 178877-32-2P **178877-33-3P** **178877-34-4P**
181574-69-6P 181574-70-9P 181574-71-0P 181574-72-1P 181574-73-2P
181574-74-3P 181574-75-4P 181574-76-5P 181574-77-6P 181574-78-7P
181574-79-8P 181574-80-1P 181574-81-2P 181574-82-3P 181574-85-6P
182957-20-6P 182957-21-7P 182957-22-8P 182957-23-9P 182957-24-0P
188638-12-2P 188638-13-3P 188638-14-4P 188638-15-5P 188638-20-2P
200351-76-4P 200351-81-1P 200351-85-5P 200351-86-6P 200351-91-3P
200351-98-0P 200352-03-0P 200352-04-1P 200352-05-2P 200352-06-3P
200352-07-4P 200352-08-5P 200352-09-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

IT 178876-99-8P 178877-27-5P 178877-28-6P 178877-29-7P 178877-30-0P
178962-97-5P 178963-05-8P 181574-86-7P 181574-88-9P 181574-89-0P
188638-07-5P 188638-11-1P 188638-19-9P 200351-75-3P 200351-87-7P
200351-89-9P 200351-90-2P 200351-99-1P 200352-10-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

IT **178877-33-3P** **178877-34-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and cytotoxic activity of analogs of CC-1065 and the

duocarmycins)
IT **178877-33-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)
RN 178877-33-3 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-8-cyano-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L31 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:783786 HCAPLUS
DN 128:48468
ED Entered STN: 15 Dec 1997
TI Preparation of DNA-binding glucuronide indoles immuno-conjugates as antitumors
IN Wang, Yuqiang; Wright, Susan C.; Larrick, James W.
PA Panorama Research, Inc., USA
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 33-8 (Carbohydrates)
Section cross-reference(s): 1, 34, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9744000	A2	19971127	WO 1997-US9055	19970522 <--
WO 9744000	A3	19971231		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5843937	A	19981201	US 1996-652883	19960523 <--
AU 9732170	A1	19971209	AU 1997-32170	19970522 <--
EP 918752	A2	19990602	EP 1997-927798	19970522 <--
R: AT, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE				
CN 1219841	A	19990616	CN 1997-194862	19970522 <--
JP 2000511893	T2	20000912	JP 1997-542898	19970522 <--
PRAI US 1996-652883	A	19960523 <--		

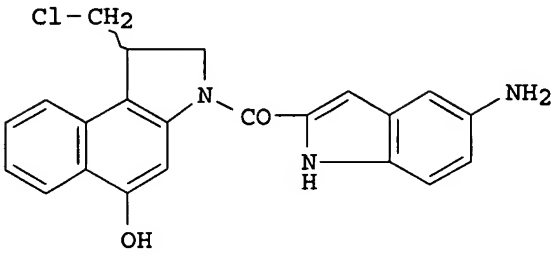
WO 1997-US9055 W 19970522 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9744000	ICM	A61K
US 5843937	ECLA	C07D403/06; C07D403/06; C07D403/14; C07D405/14; C07D495/04; C07D501/00; C07H015/24 <--

OS MARPAT 128:48468

GI



I

AB The present invention relates to novel DNA alkylating agents and the prodrugs of these agents which are useful as antitumors and DNA labeling agents. The compds. are hydroxydihydrobenzindole oligopeptides and prodrugs thereof wherein the monomeric constituents are derived from monocyclic, or bicyclic heterocyclic aromatic residues. Thus, indole I was prepared and tested for its antitumor activity with cytotoxicity (IC50 = 0.09 nM).

ST alkylating agent DNA glucuronide indole prepn; oligopeptide indole prepn antitumor cytotoxicity; DNA labeling agent glucuronide indole prepn; glucuronide indole prepn antitumor

IT Alkylation
(agents, DNA; preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT Glycosides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(glucuronides, hydroxydihydrobenzindole; preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(oligopeptides, hydroxydihydrobenzindole; preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT Antitumor agents
Cytotoxicity
(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT DNA
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT 636-47-5P, Distamycin 3 1438-30-8P, Netropsin 38099-64-8P
110314-48-2P, Adozelesin 112243-81-9P 115308-98-0P, FCE 24517
122745-33-9P 134106-78-8P 149207-46-5P 199806-22-9P 199806-30-9P
199806-31-0P 199806-32-1P **199806-33-2P** 199806-34-3P
199806-35-4P 199806-36-5P 199806-37-6P **199806-38-7P**

199806-39-8P 199806-40-1P **199806-41-2P**
199806-42-3P 199806-43-4P 199806-44-5P 199806-45-6P
199806-46-7P 199806-47-8P 199806-48-9P 199806-49-0P 199806-50-3P
199806-51-4P 199806-52-5P 199806-53-6P 199806-54-7P 199806-55-8P
199806-56-9P 199806-57-0P 199806-59-2P 199806-60-5P
199806-61-6P 199806-62-7DP, monoclonal antibody
conjugate 199806-63-8P **199806-64-9P 199806-65-0P**
199986-15-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

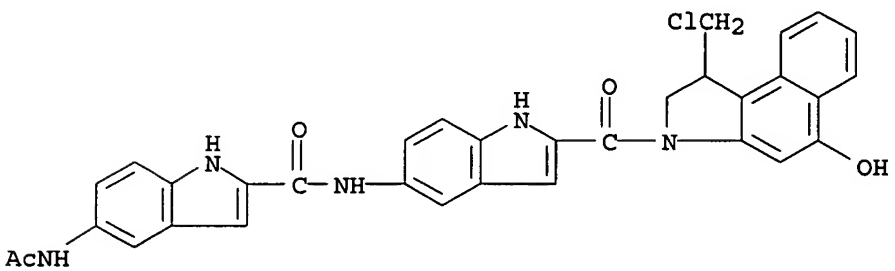
IT 496-41-3, 2-Benzofurancarboxylic acid 16732-57-3 21085-72-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT 1646-29-3P 1646-30-6P 71086-99-2P 110887-42-8P 138730-80-0P
138730-81-1P 199805-80-6P 199805-81-7P 199805-82-8P 199805-89-5P
199805-93-1P 199805-96-4P 199805-99-7P 199806-02-5P 199806-03-6P
199806-04-7P 199806-07-0P 199806-10-5P 199806-14-9P 199806-15-0P
199806-16-1P 199806-17-2P 199806-18-3P 199806-19-4P 199806-20-7P
199806-21-8P 199806-23-0P 199806-24-1P 199806-25-2P 199806-26-3P
199806-27-4P 199806-28-5P 199806-29-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT **199806-33-2P 199806-38-7P 199806-39-8P**
199806-41-2P 199806-42-3P 199806-61-6P
199806-62-7DP, monoclonal antibody conjugate **199806-64-9P**
199806-65-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT **199806-33-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

RN 199806-33-2 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-(acetylamino)-N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



L31 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:618073 HCAPLUS
DN 127:262561
ED Entered STN: 27 Sep 1997
TI synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins
IN Boger, Dale L.
PA Scripps Research Institute, USA; Boger, Dale L.
SO PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D209-70
ICS C07D403-06; C07D403-14; A61K031-40
CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9732850	A1	19970912	WO 1997-US3641	19970307 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2246783	AA	19970912	CA 1997-2246783	19970307 <--
	AU 9719902	A1	19970922	AU 1997-19902	19970307 <--
	AU 711974	B2	19991028		
	EP 888301	A1	19990107	EP 1997-908059	19970307 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2000506168	T2	20000523	JP 1997-531987	19970307 <--
	US 5985908	A	19991116	US 1998-142337	19980904 <--
PRAI	US 1996-13024P	P	19960308 <--		
	WO 1997-US3641	W	19970307 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9732850	ICM	C07D209-70
	ICS	C07D403-06; C07D403-14; A61K031-40

OS MARPAT 127:262561
GI

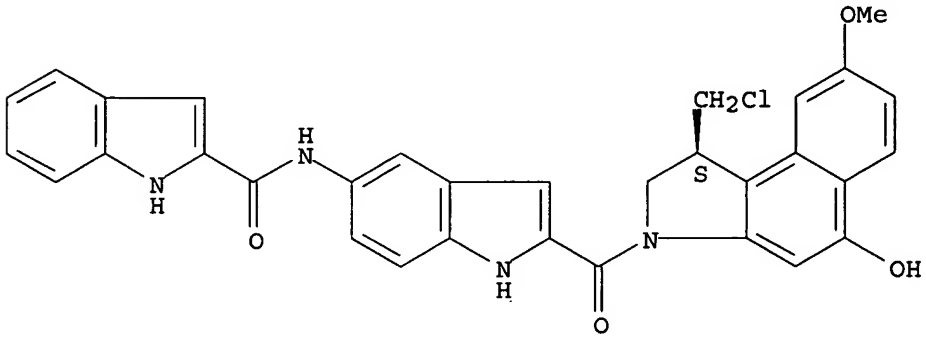
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB MCBI (7-methoxy-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one) (I) (R1 = H) is employable as a DNA alkylating agent and can be incorporated into analogs of CC-1065 and the duocarmycins I (R1 = Q1, Q2, Q3, Q4) for constructing regioselective DNA alkylating agents. Thus, I (R1 = Q1) (II) is prepared by reacting 1-(chloromethyl)-5-hydroxy-8-methoxy-1,2-dihydro-3H-benz[e]indole with Q1-CO2H followed by cyclopropanation with NaH in THF-DMF. The relative rates of DNA alkylation do not follow the relative rates of acid-catalyzed solvolysis.
ST cyclopropabenzindolone DNA alkylating agent prepn; MCBI CC 1065 duocarmycin analog prepn
IT Antitumor agents
(antibiotic; synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

IT Antibiotics
(antitumor; synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)
IT Alkylating agents, biological
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)
IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)
IT 173655-21-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)
IT 173655-22-6P 173655-25-9P 173655-26-0P 173655-27-1P 173655-28-2P
173655-29-3P 173655-30-6P 173655-31-7P 173655-32-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)
IT 173655-23-7P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)
IT 173483-64-2P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)
IT 106-95-6, Allyl bromide, reactions 123-25-1, Diethyl succinate
591-31-1, 3-Methoxybenzaldehyde 870-63-3 2564-83-2 62209-77-2
77924-28-8 101134-91-2 105518-47-6 107474-59-9 128781-07-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)
IT 151502-65-7P 157188-04-0P 173483-53-9P 173483-54-0P 173483-55-1P
173483-61-9P 173483-62-0P 173483-63-1P 173483-65-3P 173483-66-4P
173483-74-4P **173483-78-8P** 173483-82-4P 173483-86-8P
196306-01-1P 196306-02-2P 196306-03-3P 196306-04-4P 196306-10-2P
196306-21-5P 196306-22-6P 196306-23-7P 196306-25-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)
IT 92191-07-6P 196306-24-8P 196306-26-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)
IT **173483-78-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)
IT **173483-78-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)
RN 173483-78-8 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-8-methoxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L31 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:366275 HCAPLUS
DN 126:330520
ED Entered STN: 12 Jun 1997
TI Preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents
IN Boger, Dale L.
PA Scripps Research Institute, USA; Boger, Dale L.
SO PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D209-90
ICS C07D403-02; C07D403-14; C07D413-06; C07D417-06
CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1
FAN.CNT 1

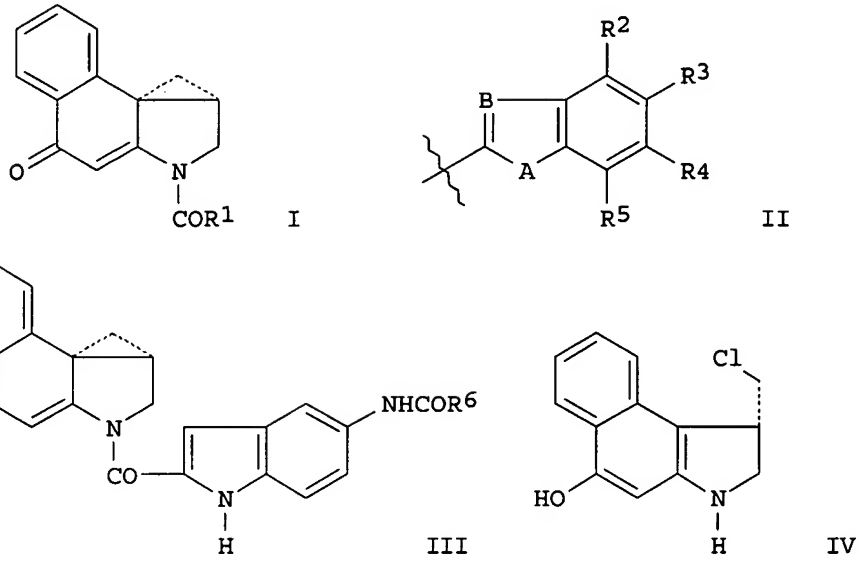
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9712862	A1	19970410	WO 1996-US16481	19961003 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
	CA 2233936	AA	19970410	CA 1996-2233936	19961003 <--
	AU 9674315	A1	19970428	AU 1996-74315	19961003 <--
	AU 727608	B2	20001214		
	EP 862553	A1	19980909	EP 1996-936498	19961003 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
	JP 11513391	T2	19991116	JP 1996-514522	19961003 <--
	NZ 321172	A	20000228	NZ 1996-321172	19961003 <--
	US 6548530	B1	20030415	US 1998-51264	19981002 <--
	US 2004002528	A1	20040101	US 2003-417043	20030415 <--
PRAI	US 1995-4752P	P	19951003 <--		
	WO 1996-US16481	W	19961003 <--		
	US 1998-51264	A1	19981002 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES

WO 9712862	ICM	C07D209-90
	ICS	C07D403-02; C07D403-14; C07D413-06; C07D417-06
US 2004002528	ECLA	C07C281/02; C07D209/42; C07D209/60; C07D209/96; C07D307/85; C07D335/06A; C07D405/12; C07D405/14; C07D405/14; C07D409/12; C07D409/12; C07D009/14; C07D409/14; C07D487/04; C07D498/04; C07D <--

GI



AB Analogs I [R1 = alkyl, amino, alkyloxy, hydrazinyl, radical (II); A = NH, O; B = C, N; R2R3 = vinylene group; R2-R3 = H, OH, alkyl, alkyloxy, pyrrolidinyl; R4-R5 = H, OH, alkyl, alkyloxy] of the antibiotics CC-1065 and the duocarmycins, containing the 1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) alkylation subunit, where prepared and shown to have potent cytotoxic activity and use as antitumor agents. Thus, amide III (R6 = 2-indolyl) was prepared starting from Me 5-nitro-2-indolecarboxylate, 2-indolecarboxylic acid and aromatic alc. IV and had an IC50 value of 10 pM when tested against L1210 cells. A direct relationship between functional stability and in vitro cytotoxic potency was shown. The CBI-based analogs were easily synthesized and were 4X more stable and 4X more potent than the corresponding analogs containing the authentic CPI alkylation subunit of CC-1065 and comparable in potency to agents containing the authentic alkylation subunit of duocarmycin SA. Similarly, the CBI-based agents alkylate DNA with an unaltered sequence selectivity at an enhanced rate and with a greater efficiency than the corresponding CPI analog and were comparable to the corresponding analog incorporating the duocarmycin SA alkylation subunit. Systematic and extensive modifications and simplifications in the DNA binding subunits attached to CBI were also described.

ST cyclopropabenzindolone duocarmycin analog prepn antitumor; duocarmycin analog prepn antitumor agent; CC1065 analog prepn antitumor agent; DNA alkylating agent duocarmycin analog prepn

IT Antitumor agents
(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT 128300-13-0P 128571-50-6P 130007-87-3P 130007-90-8P 155861-68-0P
166104-31-0P 166104-34-3P 172375-74-5P 172375-77-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT 135306-52-4P 141781-45-5P 155861-67-9P 155861-69-1P 155861-70-4P
166104-32-1P 166104-33-2P 166104-35-4P 166104-36-5P 166372-37-8P
167027-31-8P 167027-38-5P 167027-39-6P 167027-40-9P 172375-79-0P
172375-80-3P 172375-81-4P 172375-82-5P 172375-83-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT 69866-21-3, (+)-CC 1065 101222-80-4, (+)-U 71184 104713-39-5
110352-06-2 110352-07-3, (-)-CC 1065 114251-19-3 114977-72-9
118292-34-5, (+)-Duocarmycin A 127232-82-0 127306-33-6 127379-15-1
128300-14-1 128300-15-2 128300-16-3 128300-17-4 130288-24-3,
(+)-Duocarmycin SA 132746-32-8 144732-53-6 149195-48-2
149405-55-0, (-)-Duocarmycin A 151062-84-9, (-)-Duocarmycin SA
157035-50-2 157035-51-3 157922-78-6 157968-94-0 166372-38-9
172491-26-8 172491-27-9 172491-29-1 172491-30-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT 79-03-8, Propionyl chloride 99-61-6, 3-Nitrobenzaldehyde 106-95-6,
Allyl bromide, reactions 496-41-3, 2-Benzofurancarboxylic acid
555-16-8, 4-Nitrobenzaldehyde, reactions 624-83-9, Methyl isocyanate
870-46-2, tert-Butylcarbazate 1477-50-5, 1H-Indole-2-carboxylic acid
1816-92-8, Methyl 2-azidoacetate 1953-54-4, 5-Hydroxyindole 2564-83-2,
Tempo 6146-52-7, 5-Nitroindole 6314-28-9, Benzo[b]thiophene-2-carboxylic acid 7497-12-3 10242-12-3, 5-Nitrobenzofuran-2-carboxylic acid 19810-31-2, Benzyloxyacetyl chloride 38336-04-8,
2-Benzyloxyethylamine 104862-11-5, Methyl 5-Nitrobenzofuran-2-carboxylate 120506-51-6 122745-36-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT 1646-29-3P 64512-81-8P 101134-91-2P 110314-42-6P 122745-39-5P
128300-11-8P 136818-66-1P 147539-80-8P 154272-33-0P 154272-34-1P
154272-35-2P 154294-77-6P 157649-56-4P 161646-53-3P 161646-54-4P
161646-55-5P 166104-12-7P 166104-13-8P, 6H-Pyrrolo[3,2-e]benzoxazole-2-methanol 166104-14-9P 166104-15-0P 166104-16-1P 166104-18-3P
166104-19-4P 166104-20-7P 166104-21-8P 166104-22-9P 166104-23-0P
166104-24-1P 166104-25-2P 166104-26-3P 166104-27-4P 166104-28-5P
166104-37-6P 167027-28-3P 167027-29-4P 167027-30-7P 167027-32-9P
167027-33-0P 167027-34-1P 172375-67-6P 172375-68-7P 172375-69-8P
172375-70-1P 172375-71-2P 172375-72-3P 172375-85-8P 189124-88-7P
189124-89-8P 189124-90-1P 189124-91-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT 130007-86-2P 130007-89-5P **135306-53-5P** 172375-61-0P
172375-62-1P 172375-63-2P 172375-64-3P 172375-65-4P 172375-66-5P

172375-73-4P 172375-75-6P 172375-76-7P 172375-78-9P
172375-86-9P 172491-23-5P 189124-84-3P 189124-85-4P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

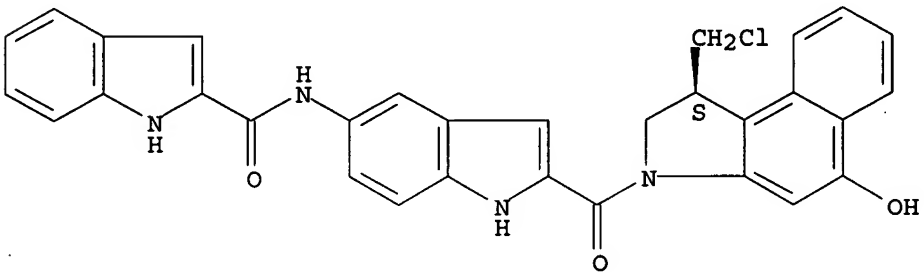
IT 166104-17-2P 172375-88-1P 172491-21-3P 172491-22-4P 172491-25-7P
189124-86-5P 189124-87-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT **135306-53-5P 172375-73-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT **135306-53-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

RN 135306-53-5 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L31 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:401674 HCAPLUS
DN 125:114357
ED Entered STN: 12 Jul 1996
TI Synthesis, Chemical Properties, and Preliminary Evaluation of Substituted CBI Analogs of CC-1065 and the Duocarmycins Incorporating the 7-Cyano-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one Alkylation Subunit: Hammett Quantitation of the Magnitude of Electronic Effects on Functional Reactivity
AU Boger, Dale L.; Han, Nianhe; Tarby, Christine M.; Boyce, Christopher W.; Cai, Hui; Jin, Qing; Kitos, Paul A.
CS Department of Chemistry, Scripps Research Institute, La Jolla, CA, 92037, USA
SO Journal of Organic Chemistry (**1996**), 61(15), 4894-4912
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English

CC 26-6 (Biomolecules and Their Synthetic Analogs)

AB The synthesis of 7-cyano-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CCBI), a substituted CBI derivative bearing a C(7) cyano group, is described in efforts that establish the magnitude of potential electronic effects on the functional reactivity of the agents. The CCBI alkylation subunit was prepared by a modified Stobbe condensation/Friedel-Crafts acylation for generation of the appropriately functionalized naphthalene precursors followed by 5-exo-trig aryl radical-alkene cyclization for synthesis of the 1,2-dihydro-3H-benz[e]indole skeleton and final Ar-3' alkylation for introduction of the activated cyclopropane. The most concise approach provided the CCBI subunit and its immediate precursor in 14-15 steps in superb overall conversions (15-20%). Resolution of an immediate CCBI precursor and its incorporation into both enantiomers of analogs of CC-1065 and the duocarmycins, are detailed. A study of the solvolysis reactivity and regioselectivity of N-BOC-CCBI revealed that introduction of the C(7) nitrile slowed the rate of solvolysis but only to a surprisingly small extent. Classical Hammett quantitation of the effect provided a remarkably small ρ (-0.3), indicating an exceptionally small C(7) substituent electronic effect on functional reactivity. Addnl. kinetic studies of acid-catalyzed nucleophilic addition proved inconsistent with C(4) carbonyl protonation as the slow and rate-determining step but consistent with a mechanism in which protonation is rapid and reversible followed by slow and rate-determining nucleophilic addition to the cyclopropane requiring both the presence and assistance of a nucleophile (SN2 mechanism). No doubt this contributes to the DNA alkylation selectivity of this class of agents and suggests that the positioning of an accessible nucleophile (adenine N-3) and not C(4) carbonyl protonation is the rate-determining step controlling the sequence selectivity of the DNA alkylation reaction. This small electronic effect on the solvolysis rate had no impact on the solvolysis regioselectivity, and stereoelectronically-controlled nucleophilic addition to the least substituted carbon of the activated cyclopropane was observed exclusively. Consistent with past studies, a direct relationship between solvolysis stability and cytotoxic potency was observed with the CCBI-derived agents providing the most potent analogs in the CBI series, and these observations were related to the predictable Hammett substituent effects. For the natural enantiomers, this unusually small electronic effect on functional reactivity had no perceptible effect on their DNA alkylation selectivity. Similar effects of the C(7) cyano substituent on the unnatural enantiomers were observed, and they proved to be 4-10 times more effective than the corresponding CBI-based unnatural enantiomers and 4-70 times less potent than the CCBI natural enantiomers.

ST cyanotetrahydrocyclopropabenzindole analog CC1065 duocarmycin prepn solvolysis; DNA alkylation cyanotetrahydrocyclopropabenzindole analog CC1065 duocarmycin

IT Inductive effect
(Hammett quantitation of the electronic effects on functional reactivity of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)

IT Deoxyribonucleic acids
RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(alkylation of DNA by cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)

IT Solvolysis
(preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)

IT 69866-21-3DP, (+)-CC-1065, analogs 118292-34-5DP, (+)-Duocarmycin A, analogs 130288-24-3DP, (+)-Duocarmycin SA, analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)

IT 178877-21-9P 178877-23-1P 178877-25-3P 178962-98-6P 178962-99-7P
178963-00-3P 178963-01-4P 178963-02-5P 178963-03-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)

IT 123-25-1, Diethyl succinate 3132-99-8, 3-Bromobenzaldehyde 62209-77-2
77924-28-8 101134-91-2 105518-47-6 128781-07-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)

IT 176442-53-8P 178876-98-7P 178876-99-8P 178877-00-4P 178877-01-5P
178877-02-6P 178877-03-7P 178877-04-8P 178877-05-9P 178877-06-0P
178877-07-1P 178877-08-2P 178877-09-3P 178877-10-6P 178877-11-7P
178877-12-8P 178877-13-9P 178877-14-0P 178877-15-1P 178877-17-3P
178877-18-4P 178877-19-5P 178877-20-8P **178877-22-0P**
178877-24-2P 178877-27-5P 178877-28-6P 178877-29-7P 178877-30-0P
178877-31-1P 178877-32-2P **178877-33-3P 178877-34-4P**
178877-35-5P 178877-36-6P 178877-37-7P 178962-96-4P 178962-97-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)

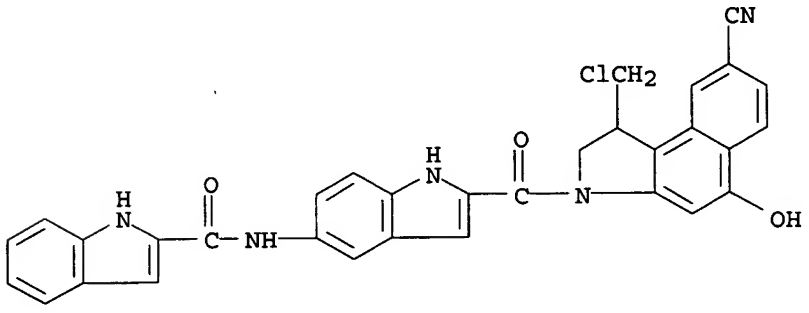
IT 178877-16-2P 178877-26-4P 178963-04-7P 178963-05-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)

IT 128300-13-0 173655-21-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(solvolysis of)

IT **178877-22-0P 178877-33-3P 178877-34-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)

IT **178877-22-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)

RN 178877-22-0 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-8-cyano-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



L31 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:113769 HCAPLUS
DN 124:175648
ED Entered STN: 23 Feb 1996
TI Synthesis and Properties of Substituted CBI Analogs of CC-1065 and the Duocarmycins Incorporating the 7-Methoxy-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (MCBI) Alkylation Subunit: Magnitude of Electronic Effects on the Functional Reactivity
AU Boger, Dale L.; McKie, Jeffrey A.; Cai, Hui; Cacciari, Barbara; Baraldi, P. G.
CS Department of Chemistry, Scripps Research Institute, La Jolla, CA, 92037, USA
SO Journal of Organic Chemistry (1996), 61(5), 1710-29
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1
AB The synthesis of 7-methoxy-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (MCBI), a substituted CBI derivative bearing a methoxy group para to the carbonyl, is described in efforts that establish the magnitude of potential electronic effects on the chemical and functional reactivity of the agents. The core structure of the MCBI alkylation subunit was prepared by a modified Stobbe condensation/Friedel-Crafts acylation for generation of the appropriately functionalized naphthalene precursors followed by 5-exo-trig aryl radical-alkene cyclization for completion of the synthesis of the 1,2-dihydro-3H-benz[e]indole skeleton and final Ar-3' alkylation for introduction of the activated cyclopropane. Two approaches to the implementation of the key 5-exo-trig free radical cyclization are detailed with the former proceeding with closure to provide the naphthindole in which the required product functionalization was introduced prior to cyclization and the latter with Tempo trap of the cyclization product of the unfunctionalized alkene substrate. The latter concise approach provided the MCBI subunit and its immediate precursor in 12-13 steps in superb overall conversions (27-30%). Resolution of an immediate MCBI precursor and its incorporation into both enantiomers of analogs of CC-1065 and the duocarmycins, are detailed. A study of the solvolysis reactivity and regioselectivity of N-BOC-MCBI revealed that introduction of the C-7 methoxy group accelerates the rate of solvolysis by only 1.2-1.06 times. This remarkably modest effect is inconsistent with C4 carbonyl protonation as the slow and rate-determining step of solvolysis or acid-catalyzed nucleophilic addition but is consistent with a mechanism in which protonation is rapid and reversible followed by slow and rate-determining nucleophilic addition to the cyclopropane requiring both the presence and assistance of a nucleophile (SN2 mechanism). No doubt this contributes to the DNA alkylation selectivity of this class of agents and suggests that the positioning of an accessible nucleophile (adenine N-3) and not C-4 carbonyl protonation is the rate-determining step controlling the sequence selectivity of the DNA alkylation reaction.
ST CBI methoxy analog prepn DNA alkylation; neoplasm inhibitor CBI methoxy analog
IT Kinetics of solvolysis
(of methoxylated CBI analogs of CC-1065)
IT Neoplasm inhibitors
(preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)
IT Deoxyribonucleic acids
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)
IT 127379-15-1 128300-13-0 132746-32-8 144732-53-6 157035-50-2

157035-51-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(kinetics of solvolysis of)

IT 173483-67-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

IT 69866-21-3DP, CC-1065, CBI analogs 173655-21-5P 173655-22-6P
173655-25-9P 173655-26-0P 173655-27-1P 173655-28-2P 173655-29-3P
173655-30-6P 173655-31-7P 173655-32-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

IT 173483-68-6P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

IT 123-25-1, Diethyl succinate 591-31-1, 3-Methoxybenzaldehyde 870-63-3
62209-77-2 77924-28-8 101134-91-2 105518-47-6 107474-59-9
128781-07-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

IT 151502-65-7P 151502-66-8P 157188-04-0P 173483-53-9P 173483-54-0P
173483-55-1P 173483-56-2P 173483-57-3P 173483-58-4P 173483-59-5P
173483-60-8P 173483-61-9P 173483-62-0P 173483-63-1P 173483-64-2P
173483-65-3P 173483-66-4P 173483-69-7P 173483-70-0P 173483-71-1P
173483-72-2P 173483-73-3P 173483-74-4P 173483-75-5P
173483-77-7P 173483-78-8P 173483-79-9P
173483-81-3P 173483-85-7P 173483-86-8P 173483-87-9P 173483-90-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

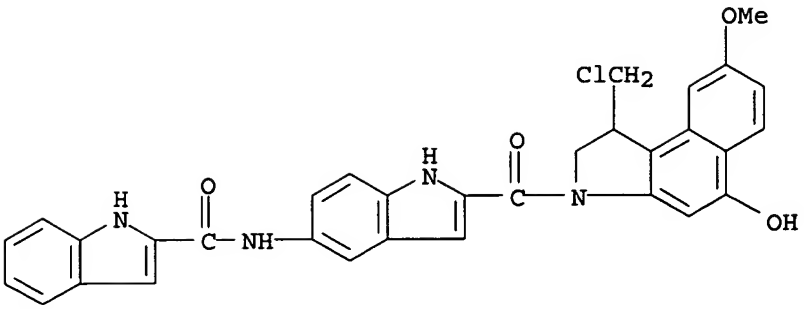
IT 173483-76-6P 173483-80-2P 173483-82-4P 173483-83-5P 173483-84-6P
173483-88-0P 173483-89-1P 173655-23-7P 173655-24-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

IT 92191-07-6P
RL: BYP (Byproduct); PREP (Preparation)
(preparation of)

IT **173483-77-7P 173483-78-8P 173483-79-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

IT **173483-77-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

RN 173483-77-7 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-8-methoxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



L31 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:981710 HCAPLUS
DN 124:86653
ED Entered STN: 13 Dec 1995
TI 1,2,9,9a-Tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) analogs of CC-1065 and the duocarmycins: synthesis and evaluation
AU Boger, Dale L.; Yun, Weiya; Han, Nianhe
CS Dep. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA
SO Bioorganic & Medicinal Chemistry (**1995**), 3(11), 1429-53
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier
DT Journal
LA English
CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1
AB An extensive study of analogs of the potent antitumor antibiotics CC-1065 and the duocarmycins which contain the 1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) alkylation subunit are detailed. In contrast to early speculation, deep-seated modifications in the CC-1065 and duocarmycin alkylation subunits are well tolerated and the CBI-based analogs proved to be potent cytotoxic agents and efficacious antitumor compds. Full details of studies defining a direct relationship between functional stability and in vitro cytotoxic potency are described. The readily accessible CBI-based analogs were four times more stable and four times more potent than the corresponding analogs containing the authentic CPI alkylation subunit of CC-1065 and comparable in potency to agents containing the authentic alkylation subunit of duocarmycin SA. Similarly, the CBI-based agents alkylate DNA with an unaltered sequence selectivity at an enhanced rate and with a greater efficiency than the corresponding CPI analog and were comparable to the corresponding analog incorporating the duocarmycin SA alkylation subunit. Systematic and extensive modifications and simplification in the DNA binding subunits attached to CBI were explored with the comparisons of both enantiomers of CC-1065 and the duocarmycins with enantiomers of many of the analogs.
ST cyclopropabenzindolone analog CC1065 duocarmycin prepn antitumor
IT Kinetics of solvolysis
(of cyclopropabenzindolone analogs of CC1065 and duocarmycins)
IT Neoplasm inhibitors
(preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)
IT 172491-26-8 172491-27-9 172491-28-0 172491-29-1 172491-30-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)
IT 69866-21-3DP, CC-1065, cyclopropabenzindolone analogs 130288-24-3DP, Duocarmycin SA, cyclopropabenzindolone analogs 155861-67-9P

155861-68-0P 155861-69-1P 172491-22-4P 172491-23-5P 172491-25-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

IT 155861-70-4P 172375-61-0P 172375-62-1P 172375-63-2P 172375-64-3P
172375-65-4P 172375-66-5P 172491-21-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

IT 135306-52-4P 141781-45-5P 172375-79-0P 172375-80-3P 172375-81-4P
172375-82-5P 172375-83-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

IT 496-41-3, 2-Benzofurancarboxylic acid 1477-50-5, 2-Indolecarboxylic acid 6314-28-9, 2-Benzothiophenecarboxylic acid 7497-12-3, Bis(2,4-dinitrophenyl) carbonate 10242-12-3, 5-Nitro-2-benzofurancarboxylic acid 107474-69-1 120506-51-6 128571-50-6, (+)-CBI 130007-86-2 130008-89-8 147539-80-8, Methyl 5-amino-2-indolecarboxylate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

IT 1646-29-3P, Methyl 5-amino-2-benzofurancarboxylate 64512-81-8P
101134-91-2P 104862-11-5P, Methyl 5-nitro-2-benzofurancarboxylate
110314-42-6P 130007-88-4P 130007-89-5P **135306-53-5P**
154272-33-0P 154272-34-1P 154272-35-2P 154294-77-6P 172375-67-6P
172375-68-7P 172375-69-8P 172375-70-1P 172375-71-2P 172375-72-3P
172375-73-4P 172375-74-5P 172375-75-6P 172375-76-7P
172375-77-8P 172375-78-9P 172375-84-7P 172375-85-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

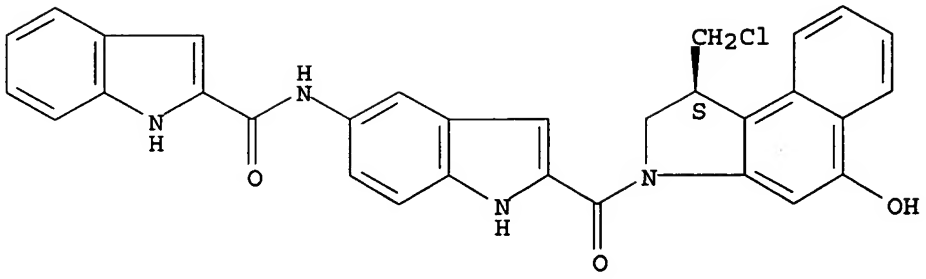
IT 172375-86-9P 172375-87-0P 172375-88-1P 172491-24-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

IT **135306-53-5P 172375-73-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

IT **135306-53-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

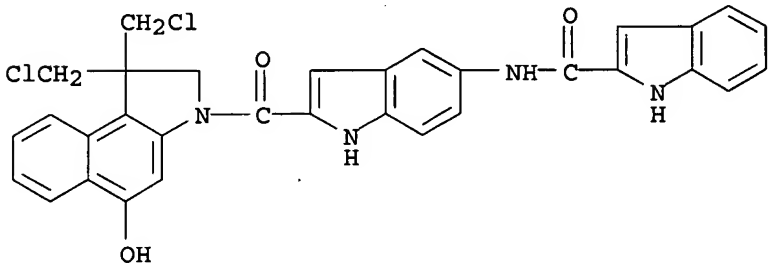
RN 135306-53-5 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L31 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:235386 HCAPLUS
DN 120:235386
ED Entered STN: 14 May 1994
TI Evaluation of functional analogs of CC-1065 and the duocarmycins incorporating the crosslinking 9a-chloromethyl-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (C2BI) alkylation subunit
AU Boger, Dale L.; Johnson, Douglas S.; Palanki, Moorthy S. S.
CS Dep. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA
SO Bioorganic & Medicinal Chemistry (**1993**), 1(1), 27-38
CODEN: BMECEP; ISSN: 0968-0896
DT Journal
LA English
CC 1-3 (Pharmacology)
AB The DNA alkylation properties and in vitro cytotoxic activity of a series of analogs of CC-1065 and the duocarmycins incorporating the 9a-chloromethyl-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (C2BI) alkylation subunit are detailed. The C2BI-based agents have been shown to alkylate DNA within the minor groove in a fashion analogous to CC-1065 or duocarmycin. The stereoelectronically controlled adenine N3 addition to the least substituted cyclopropane carbon occurs with a selectivity that represents a composite of the two enantiomers of the corresponding CBI-based agents. Addnl. high-affinity alkylation sites were detected which were not prominent alkylation sites for either enantiomer of the CBI-based agents. Such sites may represent induced high-affinity alkylation sites resulting from DNA crosslinking following complementary strand alkylation at a high-affinity alkylation site and each such site detected proved consistent with predicted models of an adenine--adenine crosslinking event. Further, consistent with this interpretation, the C2BI agents were shown to constitute efficient crosslinking agents with DNA crosslinking being observed at the same concns. as DNA alkylation. In comparison to the parent CBI-based agents, the C2BI-based agents proved to be approx. 100-10,000x less effective at DNA alkylation and 100-10,000x less potent in cytotoxic assays. This is suggested to be the consequence of a significant steric deceleration of the adenine N3 alkylation reaction attributable to the addnl. 9a-chloromethyl substituent. Consistent with this interpretation, the noncovalent binding constant of C2BI-CDPI2 for poly[dA]-poly[dT] proved nearly identical to that of CDPI3 under kinetic binding conditions, and prolonged incubation of C2BI-CDPI2 with poly[dA]-poly[dT] (72 h, 25°) provided covalent complexes with a helix stabilization comparable to that observed with (+)- or (-)-CPI-CDPI2 indicating that the size of the C2BI subunit inhibits but does not preclude productive DNA alkylation.
ST CC1065 duocarmycin DNA crosslinking chloromethyltetrahydrocyclopropabenzindolone alkylation
IT Cytotoxic agents
(CC-1065 and duocarmycin analogs as, DNA crosslinking by)
IT Deoxyribonucleic acids
RL: BIOL (Biological study)

(crosslinking, from CC-1065 and duocarmycin analogs, cytotoxicity in relation to)
IT Molecular structure-biological activity relationship
(DNA-crosslinking, of CC-1065 and duocarmycin analogs)
IT Molecular structure-biological activity relationship
(cytotoxic, of CC-1065 and duocarmycin analogs)
IT 69866-21-3D, CC-1065, analogs 118292-34-5D, Duocarmycin A, analogs
144318-47-8 144318-48-9 144318-50-3 144318-51-4 144318-52-5
144318-54-7 144318-55-8 144318-56-9 144318-57-0 144318-58-1
144318-59-2 **144318-60-5** 144318-61-6 154497-13-9
RL: BIOL (Biological study)
(DNA alkylation and cytotoxic activities of, incorporating the crosslinking chloromethyltetrahydrocyclopropa[c]benz[e]indolone alkylation subunit)
IT **144318-60-5**
RL: BIOL (Biological study)
(DNA alkylation and cytotoxic activities of, incorporating the crosslinking chloromethyltetrahydrocyclopropa[c]benz[e]indolone alkylation subunit)
IT **144318-60-5**
RL: BIOL (Biological study)
(DNA alkylation and cytotoxic activities of, incorporating the crosslinking chloromethyltetrahydrocyclopropa[c]benz[e]indolone alkylation subunit)
RN 144318-60-5 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1,1-bis(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



L31 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:651104 HCAPLUS
DN 117:251104
ED Entered STN: 26 Dec 1992
TI Functional analogs of CC-1065 and the duocarmycins incorporating the 9a-(chloromethyl)-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (C2BI) alkylation subunit: synthesis and preliminary DNA alkylation studies
AU Boger, Dale L.; Palanki, Moorthy S. S.
CS Dep. CHem., Scripps Res. Inst., La Jolla, CA, 92037, USA
SO Journal of the American Chemical Society (**1992**), 114(24), 9318-27
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1
OS CASREACT 117:251104
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A concise and effective nine to ten step synthesis of 9a-(chloromethyl)-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (I) is detailed based on the implementation of a key 5-exo-trig aryl radical-alkene cyclization for direct introduction of a selectively protected 3,3-bis(hydroxymethyl)indoline. The incorporation of I into functional analogs of CC-1065 and the duocarmycins is described. The fundamental solvolytic behavior of N-tert-butoxycarbonyl-I is detailed (t1/2 = 433 h, pH = 3) in studies which reveal that the agent is approx. 12 times more stable than the authentic alkylation subunit of CC-1065 and that it participates in the stereoelectronically-controlled reaction with nucleophilic addition to the least substituted cyclopropane carbon. Preliminary studies demonstrating the DNA alkylation and crosslinking properties of benzindole II (R = Q) and cyclopropabenzindole III (R = Q) are presented.

ST CC1065 cyclopropabenzindolone analog; chloromethylbenzindole analog CC1065; crosslinking DNA CC1065 cyclopropabenzindolone analog; DNA alkylation CC1065 cyclopropabenzindolone analog

IT Deoxyribonucleic acids
RL: PRP (Properties)
(alkylation and crosslinking of, with chloromethylcyclopropabenzindole analogs of CC-1065)

IT 56061-88-2 144345-49-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(Wittig reaction of, with phenylaminomethyl benzyloxymethyl ketone)

IT 101134-91-2 105518-47-6 107474-59-9 128781-07-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation reaction of, with chloromethylbenzindole)

IT 144318-53-6P
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(formation and amidation of, with indolecarboxylic acids)

IT 69866-21-3DP, CC-1065, chloromethylcyclopropabenzindole analogs
RL: PREP (Preparation)
(preparation and DNA alkylation and crosslinking by)

IT 144318-57-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and DNA alkylation and crosslinking by)

IT 144318-34-3P 144318-41-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and Wittig reaction of, with pyranyloxymethylenephosphorane)

IT 22539-93-1P, 1-(Benzyloxy)propan-2-one 144318-39-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and bromination of)

IT 144318-46-7P 144318-49-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and chlorination of)

IT 144318-42-3P 144318-43-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, benzindole from)

IT 144318-47-8P 144318-50-3P 144318-54-7P 144318-58-1P
144318-60-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, cyclopropabenzindolone from)

IT 144318-35-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, indoline from)

IT 144318-37-6P 144318-45-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and debenzylation of)

IT 144318-36-5P 144318-44-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and detetrahydropyranylation of)

IT 4039-82-1P, Benzyl propargyl ether
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and oxidation of, benzyloxymethyl Me ketone from)

IT 144318-51-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and solvolytic reactivity of)

IT 144318-40-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and N-alkylation of, with benzyloxymethyl bromomethyl ketone)

IT 1024-38-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and N-alkylation of, with bromomethyl benzyloxymethyl ketone)

IT 144318-38-7P 144318-48-9P 144318-52-5P 144318-55-8P 144318-59-2P 144318-61-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 144318-56-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, cyclization of, and DNA alkylation and crosslinking by)

IT 106-96-7, Propargyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with benzyl alc.)

IT 100-51-6, Benzyl alcohol, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with propargyl bromide)

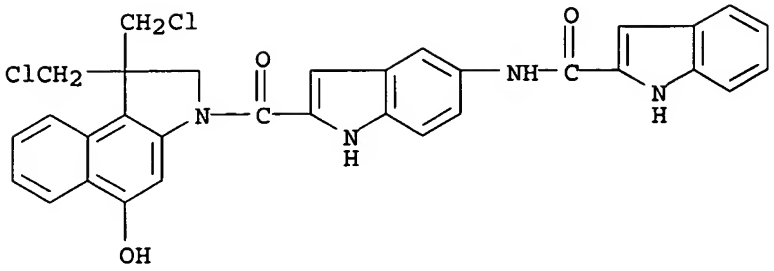
IT 615-36-1, 2-Bromoaniline 122745-35-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(tosylation of)

IT 144318-33-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-alkylation by, of tosylaniline and tosylaminonaphthalene)

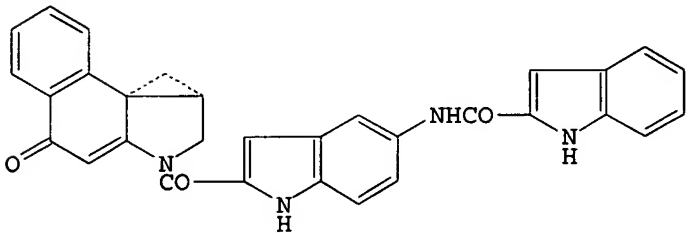
IT **144318-60-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, cyclopropabenzindolone from)

IT **144318-60-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, cyclopropabenzindolone from)

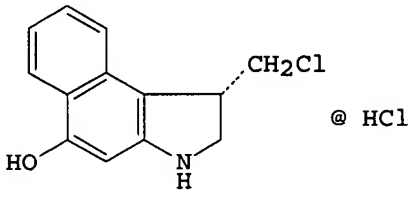
RN 144318-60-5 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1,1-bis(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



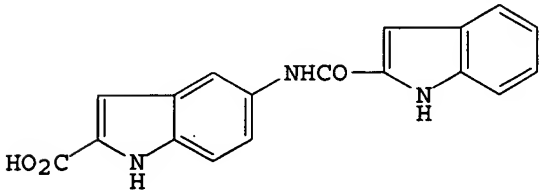
L31 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:491913 HCAPLUS
DN 115:91913
ED Entered STN: 06 Sep 1991
TI Synthesis and preliminary evaluation of (+)-CBI-indole2: an enhanced functional analog of (+)-CC-1065
AU Boger, Dale L.; Ishizaki, Takayoshi; Sakya, Subas M.; Munk, Stephen A.; Kitos, Paul A.; Jin, Qing; Besterman, Jeffrey M.
CS Dep. Chem., Purdue Univ., West Lafayette, IN, 47907, USA
SO Bioorganic & Medicinal Chemistry Letters (**1991**), 1(2), 115-20
CODEN: BMCLE8; ISSN: 0960-894X
DT Journal
LA English
CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1
GI



I



II

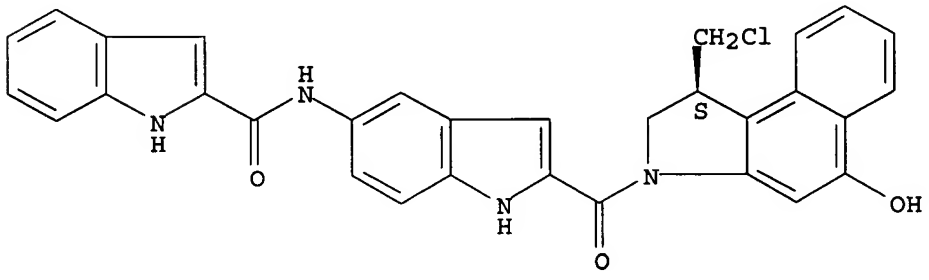


III

AB The title compound (I) was prepared from the chloromethylbenzindole II and the indolecarboxamidoindolecarboxylic acid III. I has better antitumor activity than its pyrroloindole analog.

ST cyclopropabenzindole fragment CC 1065; antitumor CC 1065 fragment
IT Neoplasm inhibitors
(cyclopropabenzindolone fragment of CC-1065)
IT 101222-80-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antitumor activity of)
IT 69866-21-3P, (+)-CC 1065
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(cyclopropabenzindole fragment of, preparation and antitumor activity of)
IT 130007-86-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(deblocking of)
IT 135306-52-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antitumor activity of)
IT **135306-53-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclopropanation of)
IT 130007-89-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with indolecarboxamidoleindolecarboxylic acid)
IT 101134-91-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with chloromethylbenzindole)
IT **135306-53-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclopropanation of)
IT **135306-53-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclopropanation of)
RN 135306-53-5 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

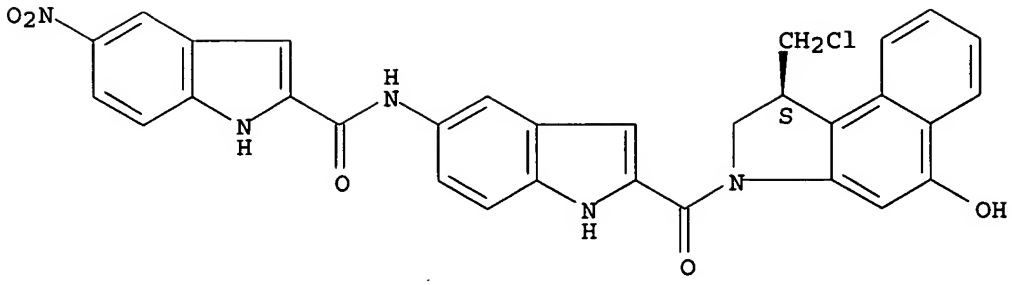
FILE 'USPAT2' ENTERED AT 15:56:47 ON 29 SEP 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> => d l37 bib abs hitrn fhitstr tot

L37 ANSWER 1 OF 12 USPATFULL on STN
AN 2004:144203 USPATFULL
TI Prodrugs of CC-1065 analogs
IN Yongxin, Robert, Watertown, MA, UNITED STATES
Chari, Ravi V.J., Newton, MA, UNITED STATES
PA IMMUNOGEN INC. (U.S. corporation)
PI US 2004109867 A1 20040610
AI US 2003-692856 A1 20031027 (10)
RLI Division of Ser. No. US 2002-116053, filed on 5 Apr 2002, PENDING
DT Utility
FS APPLICATION
LREP SUGHRUE MION, PLLC, 2100 PENNSYLVANIA AVENUE, N.W., SUITE 800, WASHINGTON, DC, 20037
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 1134
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Prodrugs of analogs of the anti-tumor antibiotic CC-1065 having a cleavable protective group such as a piperazino carbamate, a 4-piperidino-piperidino carbamate or a phosphate, in which the protecting group confers enhanced water solubility and stability upon the prodrug, and in which the prodrug also has a moiety, such as a disulfide, that can conjugate to a cell binding reagent such as an antibody. The therapeutic use of such prodrug conjugates is also described; such prodrugs of cytotoxic agents have therapeutic use because they can deliver cytotoxic prodrugs to a specific cell population for enzymatic conversion to cytoxic drugs in a targeted fashion.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **501441-05-0P 501666-85-9P 615538-42-6P**
615538-45-9P 615538-47-1P 615538-49-3P
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
IT **615538-44-8P 615538-46-0P 615538-48-2P**
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
IT **615538-51-7P 615538-52-8P**
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
IT **615538-53-9P 615538-54-0P 615538-55-1P**
615538-56-2P 615538-57-3DP, salt **615538-58-4P**
615538-59-5DP, salt
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
IT **501441-05-0P**
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
RN 501441-05-0 USPATFULL
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



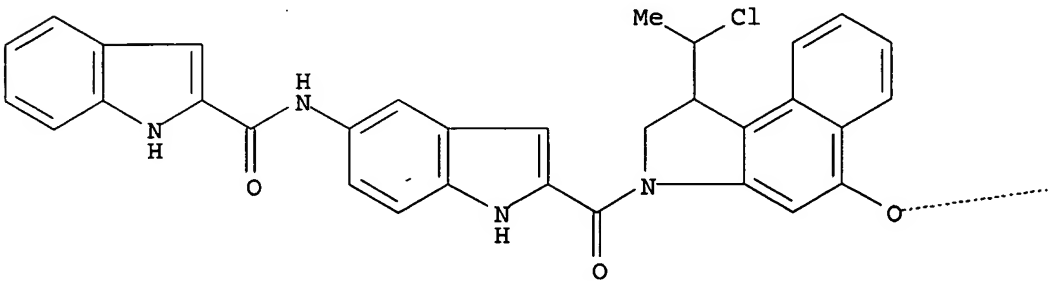
L37 ANSWER 2 OF 12 USPATFULL on STN
AN 2004:44969 USPATFULL
TI Novel prodrugs von 6-hydroxy-2,3-dihydro-1h-indoles, 5-hydroxy-1,2-dihydro-3h-pyrrolo[3,2-e]indoles and 5-hydroxy-1,2-dihydro-3h-benzo(e)indoles as well as of 6-hydroxy-1,2,3,4-tetrahydro-benzo[f]quinoline derivatives for use in selective cancer therapy
IN Tietze, Lutz F., Gottingen, GERMANY, FEDERAL REPUBLIC OF
Herzig, Tobias, Marsstr, GERMANY, FEDERAL REPUBLIC OF
Fecher, Anja, Eisenbahnstr.16, GERMANY, FEDERAL REPUBLIC OF
PI US 2004033962 A1 20040219
AI US 2003-275415 A1 20030630 (10)
WO 2001-EP4904 20010502
PRAI DE 2000-100 20000502
DE 2000-100 20000523
DT Utility
FS APPLICATION
LREP Stephan A Pendorf, Pendorff & Cutliff, PO Box 20445, Tampa, FL, 33622-0445
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1047
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The chemotherapy of malignant tumours is greatly restricted by the generally slight differentiation of the available cytostatic agents between normal and malignant tissue. In order to achieve an improvement of the selectivity in cancer therapy, novel prodrugs have been developed from 6-hydroxy-2,3-dihydro-1H-indolene, 5-hydroxy-1,2-dihydro-3H-pyrrolo[3,2-e]indolene and 5-hydroxy-1,2-dihydro-3H-benzo[e]indolene as well as from 6-hydroxy-1,2,3,4-tetrahydro-benzo[f]-quinolines, that may be used within the framework of the ADEP therapy (antibody directed enzyme prodrug therapy). The new prodrugs are characterised by a high difference in toxicity between the prodrug and underlying drug and by a very high efficacy of the drug. The high selectivity of the new prodrugs is probably attributed to the fact that, in the new prodrugs, a secondary halide is present in contrast to the prodrugs of a similar type previously produced by us. The direct alkylation of the DNA or RNA by the prodrugs and thus the toxicity of the prodrugs is thereby reduced. After splitting off of the glycosidic and/or acetal group on the phenolic hydroxy groups of the prodrugs, a spirocyclopropacyclohexadiene is formed which, being a highly toxic group, effects an alkylation of the DNA or RNA.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **330206-90-1P**
(preparation of glycosidic prodrugs containing substituted indolenes for use in
cancer therapy)
IT **330206-89-8P**

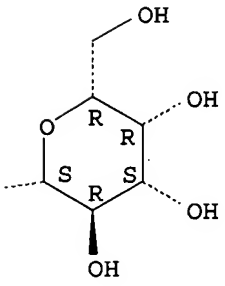
(preparation of glycosidic prodrugs containing substituted indolenes for use in
cancer therapy)
IT **330206-90-1P**
(preparation of glycosidic prodrugs containing substituted indolenes for use in
cancer therapy)
RN 330206-90-1 USPATFULL
CN 1H-Indole-2-carboxamide, N-[2-[[1-(1-chloroethyl)-5-(β-D-galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

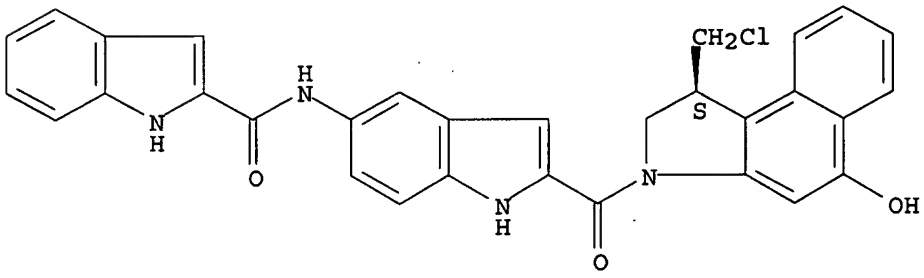


L37 ANSWER 3 OF 12 USPATFULL on STN
AN 2004:2505 USPATFULL
TI CBI analogs of CC-1065 and the duocarmycins
IN Boger, Dale L., La Jolla, CA, UNITED STATES
PA The Scripps Research Institute, La Jolla, CA, UNITED STATES (U.S. corporation)
PI US 2004002528 A1 20040101
AI US 2003-417043 A1 20030415 (10)
RLI Continuation of Ser. No. US 1998-51264, filed on 2 Oct 1998, GRANTED, Pat. No. US 6548530 A 371 of International Ser. No. WO 1996-US16481, filed on 3 Oct 1996, PENDING
PRAI US 1995-4752P 19951003 (60)
DT Utility
FS APPLICATION
LREP THE SCRIPPS RESEARCH INSTITUTE, OFFICE OF PATENT COUNSEL, TPC-8, 10550 NORTH TORREY PINES ROAD, LA JOLLA, CA, 92037
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 34 Drawing Page(s)
LN.CNT 2984
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Analogs of the antitumor antibiotics CC-1065 and the duocarmycins incorporate the 1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) alkylation subunit. The CBI-based analogs have potent cytotoxic activity and are useful as efficacious antitumor compounds. A direct relationship between functional stability and in vitro cytotoxic potency is disclosed. The CBI-based analogs are easily synthesized and are 4+ more stable and 4+ more potent than the corresponding analogs containing the authentic CPI alkylation subunit of CC-1065 and comparable in potency to agents containing the authentic alkylation subunit of duocarmycin SA. Similarly, the CBI-based agents alkylate DNA with an unaltered sequence selectivity at an enhanced rate and with a greater efficiency than the corresponding CPI analog and were comparable to the corresponding analog incorporating the duocarmycin SA alkylation subunit. Systematic and extensive modifications and simplifications in the DNA binding subunits attached to CBI are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **135306-53-5P 172375-73-4P**
(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)
IT **135306-53-5P**
(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)
RN 135306-53-5 USPATFULL
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

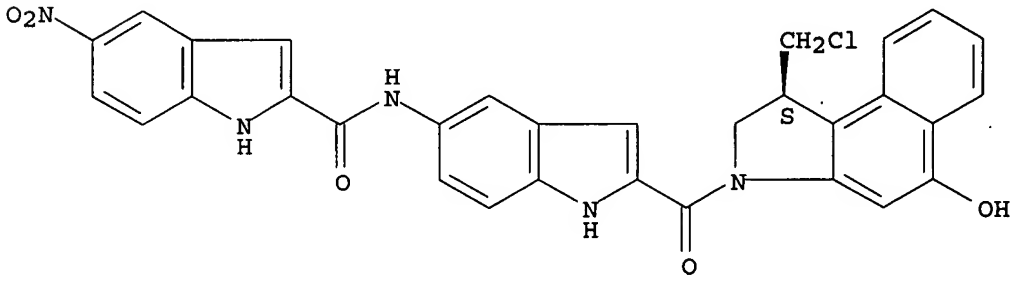


L37 ANSWER 4 OF 12 USPATFULL on STN
AN 2003:283175 USPATFULL
TI Prodrugs of CC-1065 analogs
IN Zhao, Robert Yongxin, Watertown, MA, UNITED STATES
Chari, Ravi V.J., Newton, MA, UNITED STATES
PA IMMUNOGEN INC. (U.S. corporation)
PI US 2003199519 A1 20031023
US 6756397 B2 20040629
AI US 2002-116053 A1 20020405 (10)
DT Utility
FS APPLICATION
LREP SUGHRUE MION, PLLC, 2100 Pennsylvania Avenue, NW, Washington, DC, 20037-3213
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 1140
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Prodrugs of analogs of the anti-tumor antibiotic CC-1065 having a cleavable protective group such as a piperazino carbamate, a

4-piperidino-piperidino carbamate or a phosphate, in which the protecting group confers enhanced water solubility and stability upon the prodrug, and in which the prodrug also has a moiety, such as a disulfide, that can conjugate to a cell binding reagent such as an antibody. The therapeutic use of such prodrug conjugates is also described; such prodrugs of cytotoxic agents have therapeutic use because they can deliver cytotoxic prodrugs to a specific cell population for enzymatic conversion to cytoxic drugs in a targeted fashion.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **501441-05-0P 501666-85-9P 615538-42-6P**
615538-45-9P 615538-47-1P 615538-49-3P
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
IT **615538-44-8P 615538-46-0P 615538-48-2P**
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
IT **615538-51-7P 615538-52-8P**
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
IT **615538-53-9P 615538-54-0P 615538-55-1P**
615538-56-2P 615538-57-3DP, salt **615538-58-4P**
615538-59-5DP, salt
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
IT **501441-05-0P**
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
RN 501441-05-0 USPATFULL
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



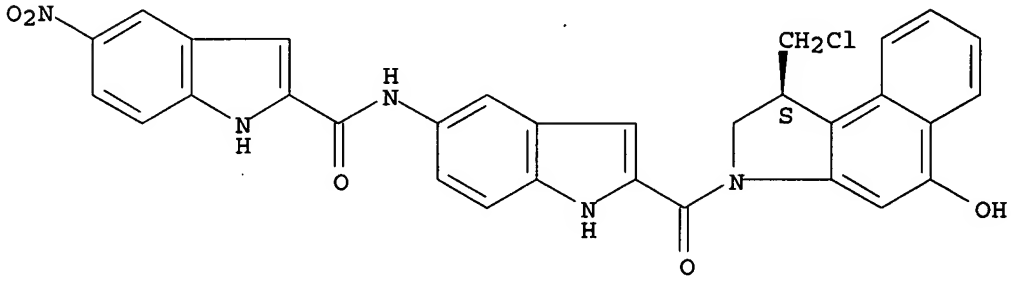
L37 ANSWER 5 OF 12 USPATFULL on STN
AN 2003:277338 USPATFULL
TI CC-1065 analog synthesis
IN Zhao, Robert Yongxin, Watertown, MA, UNITED STATES
Chari, Ravi V.J., Newton, MA, UNITED STATES
PA IMMUNOGEN INC. (U.S. corporation)
PI US 2003195365 A1 20031016
AI US 2002-265452 A1 20021007 (10)
RLI Division of Ser. No. US 2002-116052, filed on 5 Apr 2002, GRANTED, Pat. No. US 6534660
DT Utility
FS APPLICATION
LREP SUGHRUE MION, PLLC, 2100 PENNSYLVANIA AVENUE, N.W., WASHINGTON, DC, 20037
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 890
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Improved synthesis of seco(-)CBI (5-hydroxy-3-amino-1-[S]-(chloromethyl)-1,2-dihydro-3H-benz(e)indole): ##STR1##

and improved syntheses therefrom of a wide variety of CC-1065 analogs that comprise a cyclopropabenzidole (CBI) alkylating moiety, and which are collectively DC1 and its derivatives, for the synthesis of cell-targeted therapeutic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **501441-05-0P**, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole (intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)
IT **501666-85-9P 501666-87-1P**
(target product; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)
IT **501441-05-0P**, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole (intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)
RN 501441-05-0 USPATFULL
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



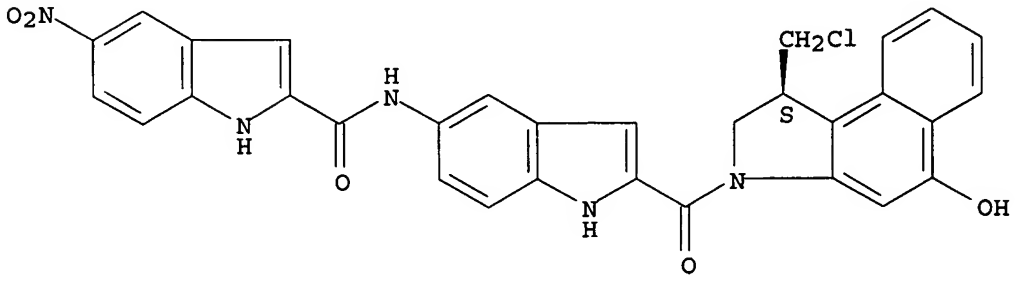
L37 ANSWER 6 OF 12 USPATFULL on STN
AN 2003:176513 USPATFULL
TI CC-1065 analog synthesis
IN Zhao, Robert Yongxin, Watertown, MA, United States
Chari, Ravi V. J., Newton, MA, United States
PA Immunogen Inc., Cambridge, MA, United States (U.S. corporation)
PI US 6586618 B1 20030701
AI US 2002-265329 20021007 (10)
RLI Division of Ser. No. US 2002-116052, filed on 5 Apr 2002
DT Utility
FS GRANTED
EXNAM Primary Examiner: McKane, Joseph K.; Assistant Examiner: Saeed, Kamal
LREP Sughrue Mion, PLLC
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 837
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Improved synthesis of seco(-)CBI (5-hydroxy-3-amino-1-[S]-(chloromethyl)-1,2-dihydro-3H-benz(e)indole): ##STR1##

and improved syntheses therefrom of a wide variety of CC-1065 analogs that comprise a cyclopropabenzidole (CBI) alkylating moiety, and which

are collectively DC1 and its derivatives, for the synthesis of cell-targeted therapeutic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **501441-05-0P**, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole (intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)
IT **501666-85-9P 501666-87-1P**
(target product; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)
IT **501441-05-0P**, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole (intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)
RN 501441-05-0 USPATFULL
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

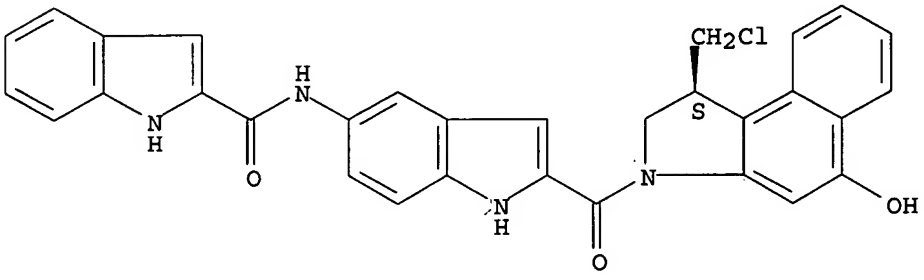


L37 ANSWER 7 OF 12 USPATFULL on STN
AN 2003:102391 USPATFULL
TI CBI analogs of CC-1065 and the duocarmycins
IN Boger, Dale L., La Jolla, CA, United States
PA The Scripps Research Institute, La Jolla, CA, United States (U.S. corporation)
PI US 6548530 B1 20030415
WO 9712862 19970410
AI US 1998-51264 19981002 (9)
WO 1996-US16481 19961003
PRAI US 1995-4752P 19951003 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Stockton, Laura L.
LREP Lewis, Donald G.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 41 Drawing Figure(s); 34 Drawing Page(s)
LN.CNT 2950
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Analogs of the antitumor antibiotics CC-1065 and the duocarmycins incorporate the 1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) alkylation subunit. The CBI-based analogs have potent cytotoxic activity and are useful as efficacious antitumor compounds. A direct relationship between functional stability and in vitro cytotoxic potency is disclosed. The CBI-based analogs are easily synthesized and are 4+ more stable and 4+ more potent than the corresponding analogs containing the authentic CPI alkylation subunit of CC-1065 and

comparable in potency to agents containing the authentic alkylation subunit of duocarmycin SA. Similarly, the CBI-based agents alkylate DNA with an unaltered sequence selectivity at an enhanced rate and with a greater efficiency than the corresponding CPI analog and were comparable to the corresponding analog incorporating the duocarmycin SA alkylation subunit. Systematic and extensive modifications and simplifications in the DNA binding subunits attached to CBI are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **135306-53-5P 172375-73-4P**
(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)
IT **135306-53-5P**
(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)
RN 135306-53-5 USPATFULL
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L37 ANSWER 8 OF 12 USPATFULL on STN
AN 2003:74493 USPATFULL
TI CC-1065 analog synthesis
IN Yongxin, Robert, Watertown, MA, United States
Chari, Ravi V. J., Newton, MA, United States
PA Immunogen, Inc., Cambridge, MA, United States (U.S. corporation)
PI US 6534660 B1 20030318
AI US 2002-116052 20020405 (10)
DT Utility
FS GRANTED
EXNAM Primary Examiner: McKane, Joseph K.; Assistant Examiner: Murphy, Jennifer C.
LREP Sughrue Mion, PLLC
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 851
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Improved synthesis of seco(-)CBI (5-hydroxy-3-amino-1-[S]-(chloromethyl)-1,2 -dihydro-3H-benz(e)indole): ##STR1##

and improved syntheses therefrom of a wide variety of CC-1065 analogs that comprise a cyclopropabenzidole (CBI) alkylating moiety, and which are collectively DC1 and its derivatives, for the synthesis of cell-targeted therapeutic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **501441-05-0P**, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[(5-nitroindol-2-

yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole (intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

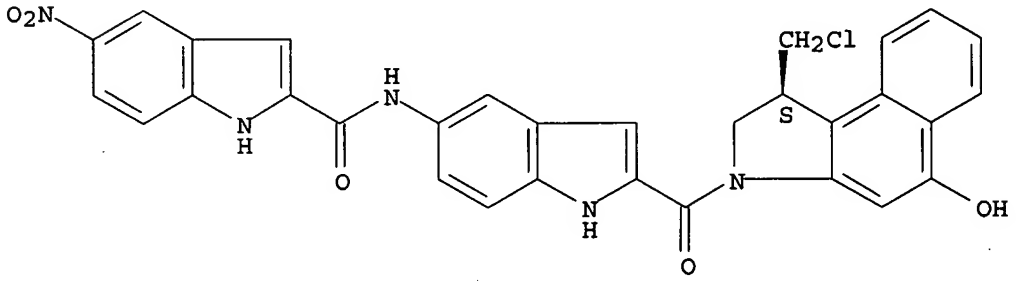
IT **501666-85-9P 501666-87-1P** (target product; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT **501441-05-0P**, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole (intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

RN 501441-05-0 USPATFULL

CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L37 ANSWER 9 OF 12 USPATFULL on STN

AN 2000:57902 USPATFULL

TI Analogs of CC-1065 and the duocarmycins

IN Boger, Dale L., La Jolla, CA, United States

PA The Scripps Research Institute, La Jolla, CA, United States (U.S. corporation)

PI US 6060608 20000509
WO 9745411 19971204

AI US 1999-194467 19990907 (9)
WO 1997-US9076 19970530
19990907 PCT 371 date
19990907 PCT 102(e) date

PRAI US 1996-18860P 19960531 (60)
US 1996-23346P 19960912 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Stockton, Laura L.

LREP Lewis, Donald G.

CLMN Number of Claims: 7

ECL Exemplary Claim: 1

DRWN 45 Drawing Figure(s); 35 Drawing Page(s)

LN.CNT 3201

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

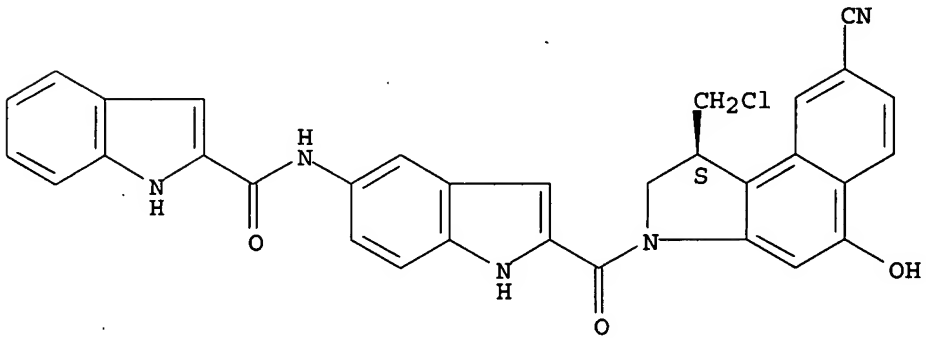
AB Analogs of antitumor antibiotics CC-1065 and the duocarmycins are synthesized which possess systematic and extensive modifications in the DNA binding subunits attached to a 1,2,9,9a-tetra-hydro-cyclopropa[c]benz[e]indol-4-one (CBI) alkylation subunit. The analogs have potent cytotoxic activity and are efficacious antitumor compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **178877-33-3P 178877-34-4P** (synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

IT **178877-33-3P**
(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)
RN 178877-33-3 USPATFULL
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-8-cyano-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

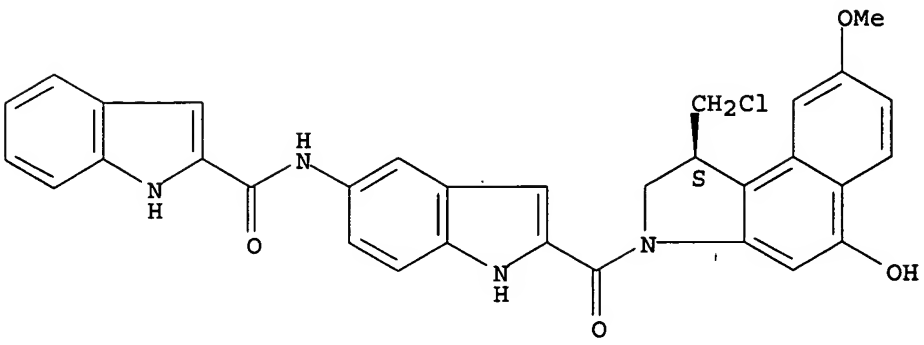
Absolute stereochemistry. Rotation (+).



L37 ANSWER 10 OF 12 USPATFULL on STN
AN 1999:146607 USPATFULL
TI MCBI analogs of CC-1065 and the duocarmycins
IN Boger, Dale L., La Jolla, CA, United States
PA The Scripps Research Institute, La Jolla, CA, United States (U.S. corporation)
PI US 5985908 19991116
WO 9732850 19970912
AI US 1998-142337 19980904 (9)
WO 1997-US3641 19970307
19980904 PCT 371 date
19980904 PCT 102(e) date
PRAI US 1996-13024P 19960308 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Gerstl, Robert
LREP Lewis, Donald G.
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 18 Drawing Figure(s); 20 Drawing Page(s)
LN.CNT 1985
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB MCBI (7-methoxy-1,2,9a-tetra-hydrocyclopropa[c]benz[e]indol-4-one) is employable as a DNA alkylating agent and can be incorporated into analogs of CC-1065 and the duocarmycins for constructing regioselective DNA alkylating agents.

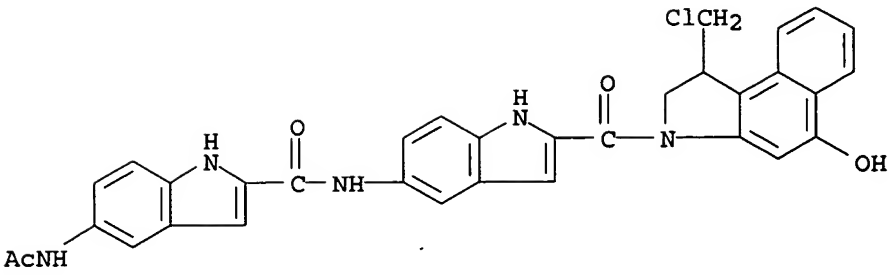
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **173483-78-8P**
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)
IT **173483-78-8P**
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)
RN 173483-78-8 USPATFULL
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-8-methoxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L37 ANSWER 11 OF 12 USPATFULL on STN
AN 1998:150939 USPATFULL
TI DNA-binding indole derivatives, their prodrugs and immunoconjugates as anticancer agents
IN Wang, Yuqiang, Mountain View, CA, United States
Wright, Susan C., Saratoga, CA, United States
Larrick, James W., Woodside, CA, United States
PA Panorama Research, Inc., Mountain View, CA, United States (U.S. corporation)
PI US 5843937 19981201
AI US 1996-652883 19960523 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Raymond, Richard L.
LREP Townsend and Townsend and Crew LLP
CLMN Number of Claims: 41
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 1644
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel DNA alkylating agents and the prodrugs of these agents which are useful as antitumor agents and DNA labelling agents. The compounds are hydroxy dihydrobenzindole oligopeptides and prodrugs thereof wherein the monomeric constituents are derived from monocyclic or bicyclic heterocyclic aromatic residues.

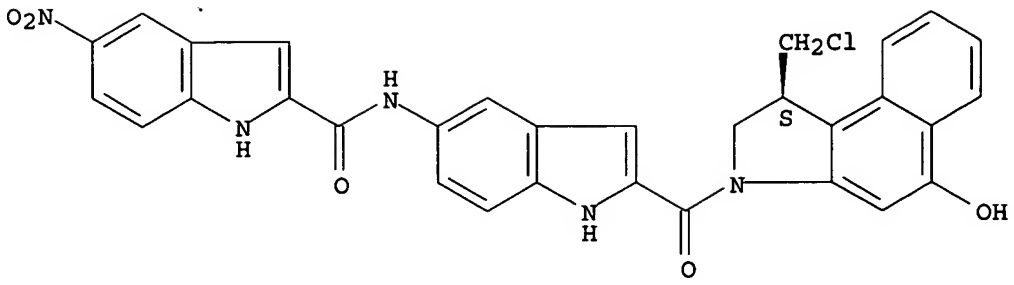
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **199806-33-2P 199806-38-7P 199806-39-8P**
199806-41-2P 199806-42-3P 199806-61-6P
199806-62-7DP, monoclonal antibody conjugate **199806-64-9P**
199806-65-0P
(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)
IT **199806-33-2P**
(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)
RN 199806-33-2 USPATFULL
CN 1H-Indole-2-carboxamide, 5-(acetylamino)-N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



L37 ANSWER 12 OF 12 USPAT2 on STN
AN 2003:283175 USPAT2
TI Prodrugs of CC-1065 analogs
IN Zhao, Robert Yongxin, Watertown, MA, United States
Chari, Ravi V. J., Newton, MA, United States
PA Immunogen, Inc., Cambridge, MA, United States (U.S. corporation)
PI US 6756397 B2 20040629
AI US 2002-116053 20020405 (10)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Desai, R; Assistant Examiner: Shiao, Robert
LREP Sughrue Mion, PLLC
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 1086
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Prodrugs of analogs of the anti-tumor antibiotic CC-1065 having a cleavable protective group such as a piperazino carbamate, a 4-piperidino-piperidino carbamate or a phosphate, in which the protecting group confers enhanced water solubility and stability upon the prodrug, and in which the prodrug also has a moiety, such as a disulfide, that can conjugate to a cell binding reagent such as an antibody. The therapeutic use of such prodrug conjugates is also described; such prodrugs of cytotoxic agents have therapeutic use because they can deliver cytotoxic prodrugs to a specific cell population for enzymatic conversion to cytoxic drugs in a targeted fashion.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **501441-05-0P 501666-85-9P 615538-42-6P**
615538-45-9P 615538-47-1P 615538-49-3P
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
IT **615538-44-8P 615538-46-0P 615538-48-2P**
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
IT **615538-51-7P 615538-52-8P**
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
IT **615538-53-9P 615538-54-0P 615538-55-1P**
615538-56-2P 615538-57-3DP, salt **615538-58-4P**
615538-59-5DP, salt
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
IT **501441-05-0P**
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
RN 501441-05-0 USPAT2
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6
DICTIONARY FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

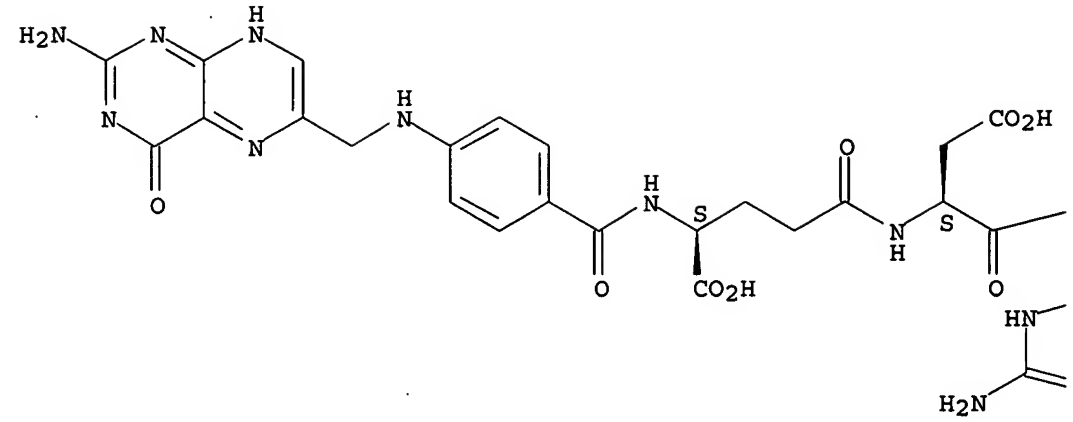
Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> => d ide can tot l26

L26 ANSWER 1 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 743424-19-3 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS STEREOSEARCH
MF C92 H98 Cl N23 O27 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES
(Uses)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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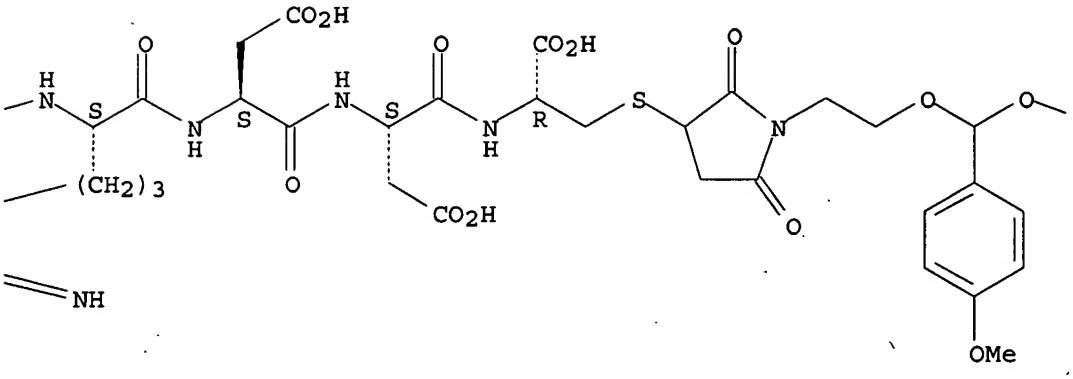

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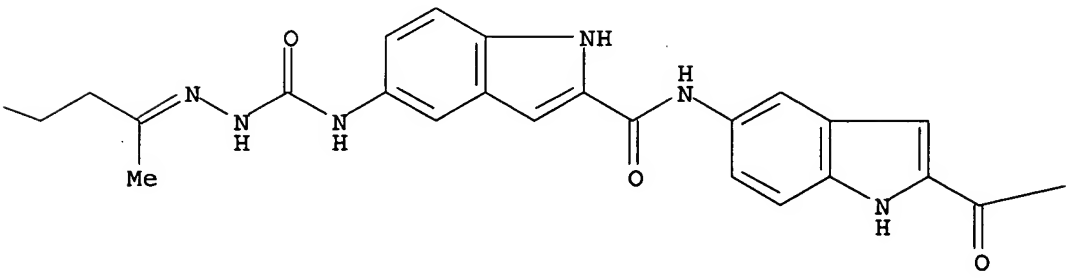

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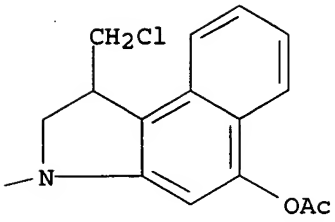

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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:207525

L26 ANSWER 2 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 742092-08-6 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
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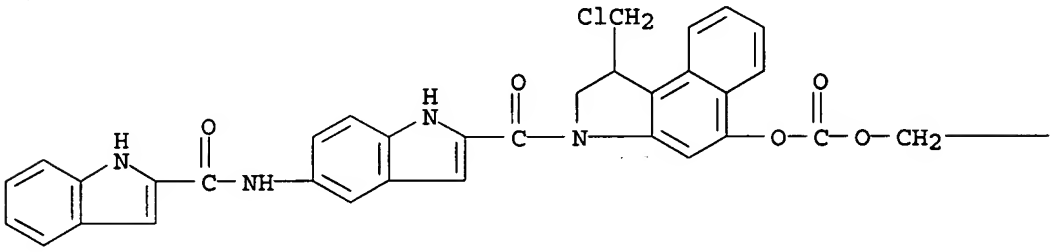
MF C39 H30 Cl N5 O5 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

PAGE 1-A



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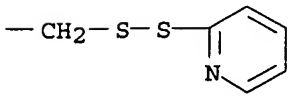

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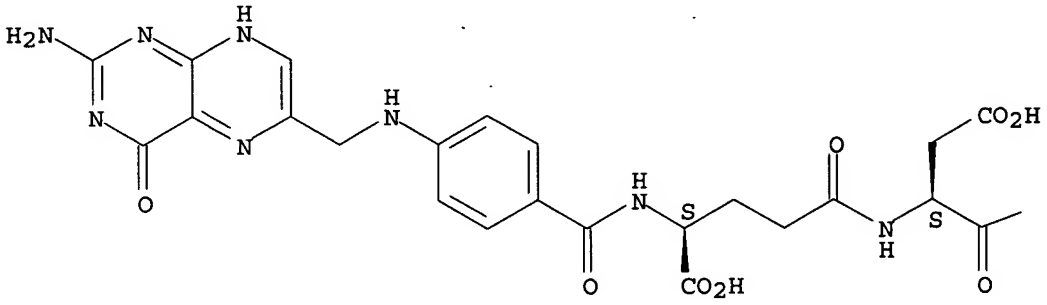
L26 ANSWER 3 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 742092-07-5 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS STEREOSEARCH
MF C91 H96 Cl N23 O24 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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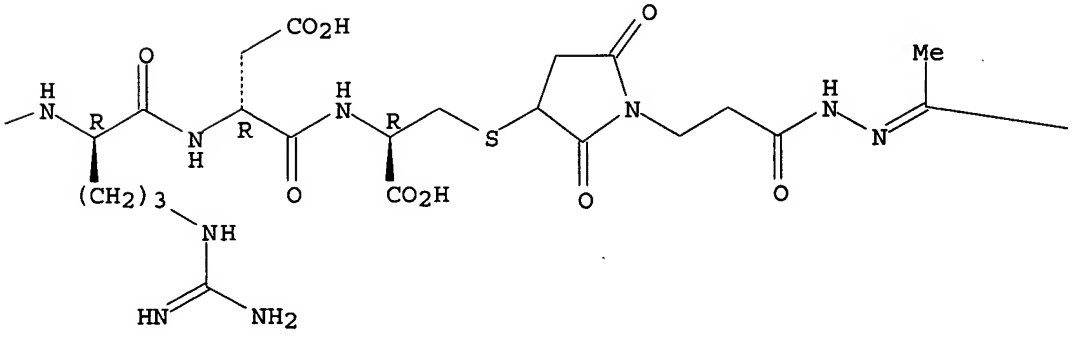

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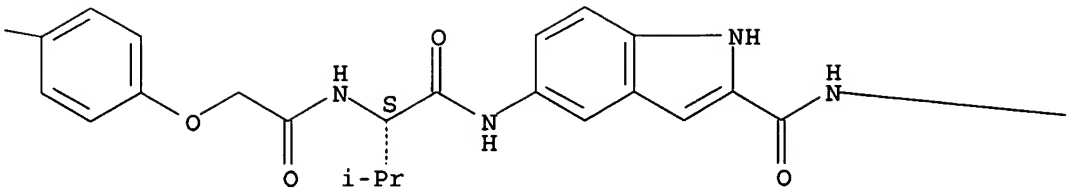

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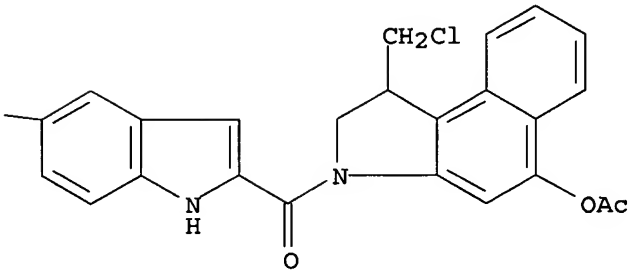

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REFERENCE 1: 141:207525

L26 ANSWER 4 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 742092-06-4 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
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SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
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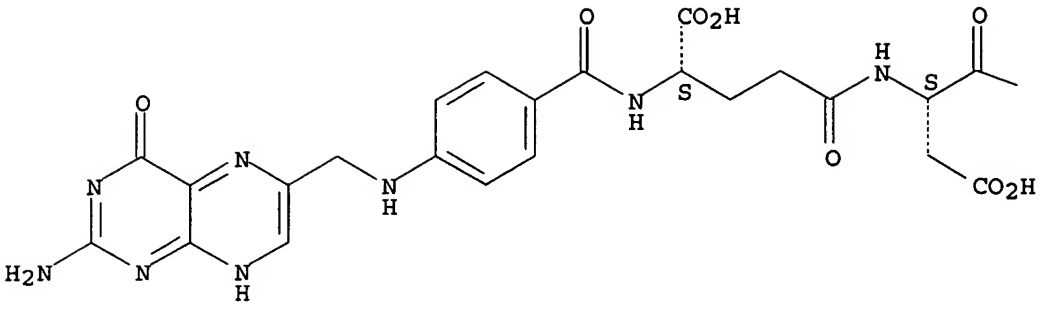
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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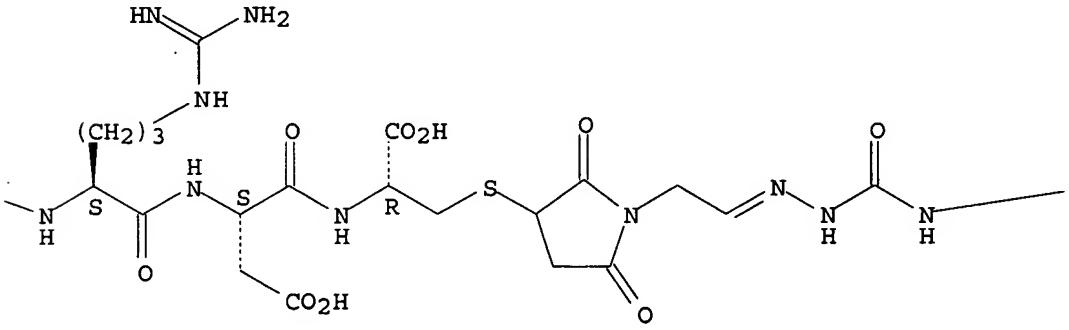

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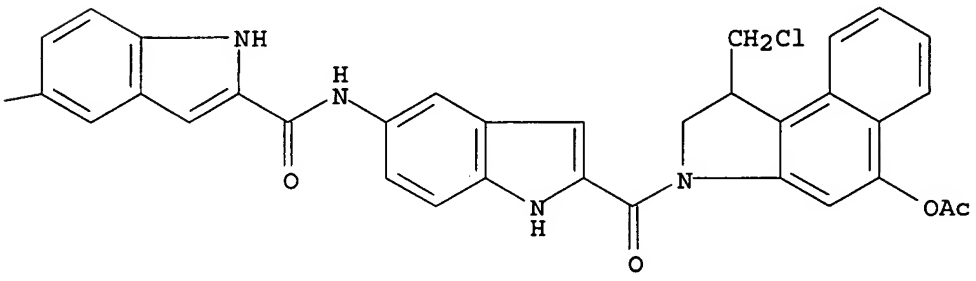

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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L26 ANSWER 5 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 742092-05-3 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
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MF C90 H94 Cl N23 O23 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
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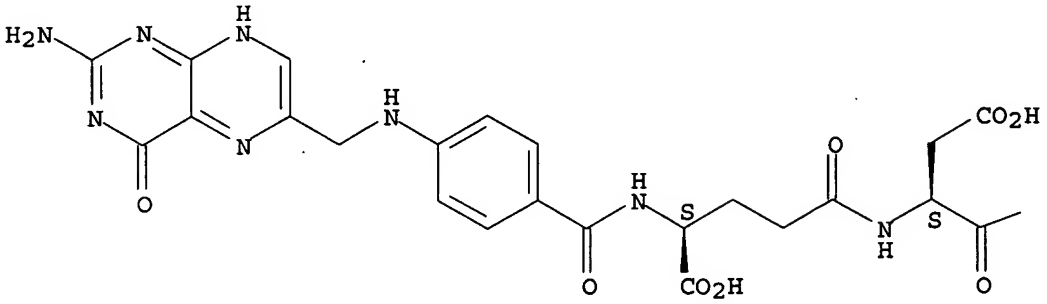
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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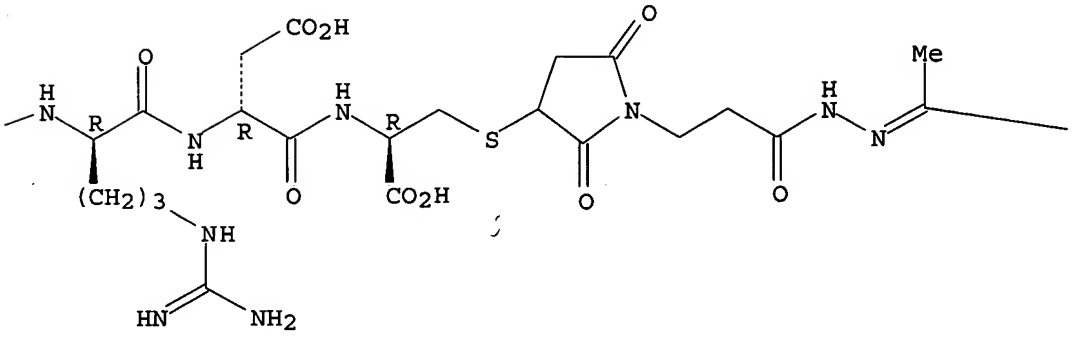

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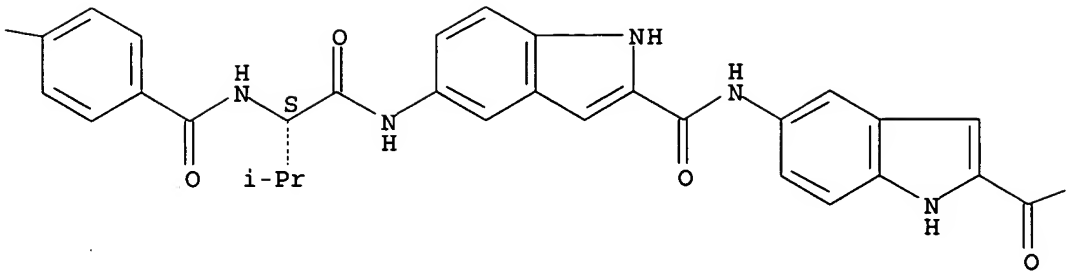

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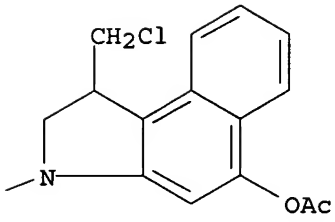

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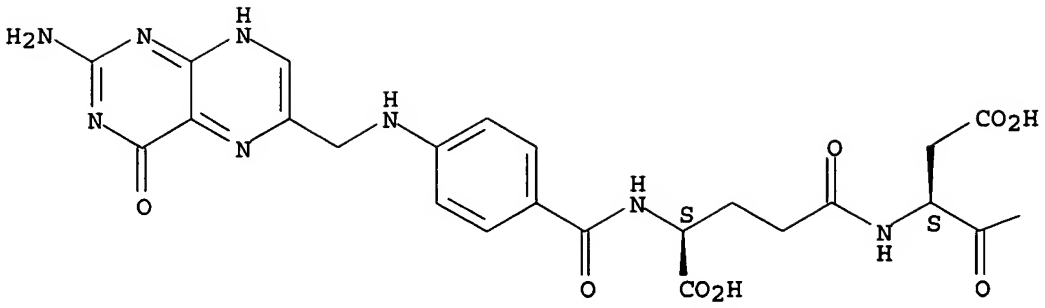
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:207525

L26 ANSWER 6 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 742092-02-0 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS STEREOSEARCH
MF C86 H94 Cl N23 O23 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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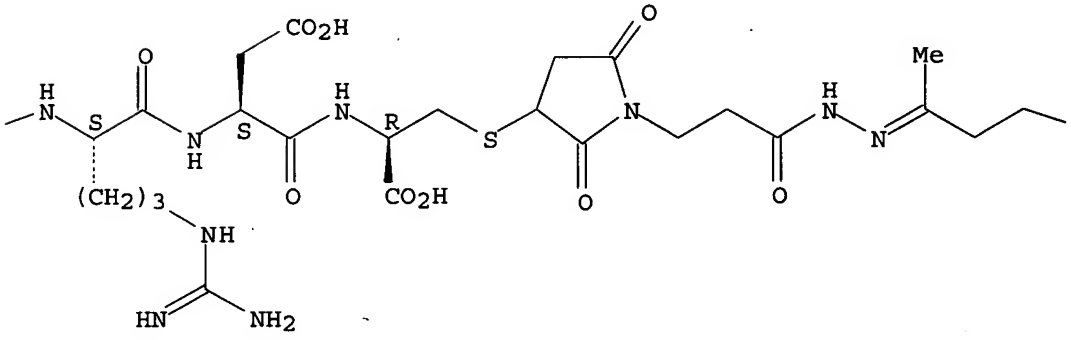

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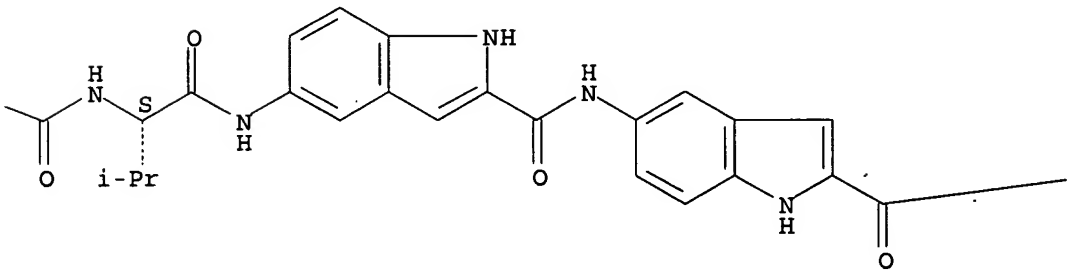

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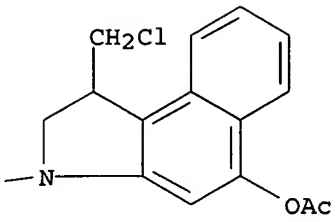

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:207525

L26 ANSWER 7 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 742091-92-5 REGISTRY
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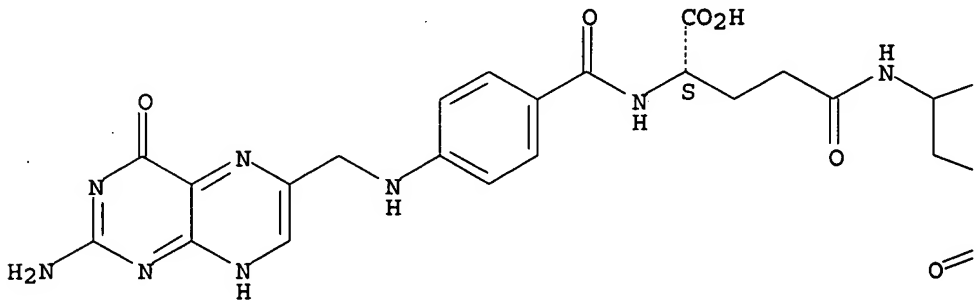
FS STEREOSEARCH
MF C65 H63 Cl N16 O17 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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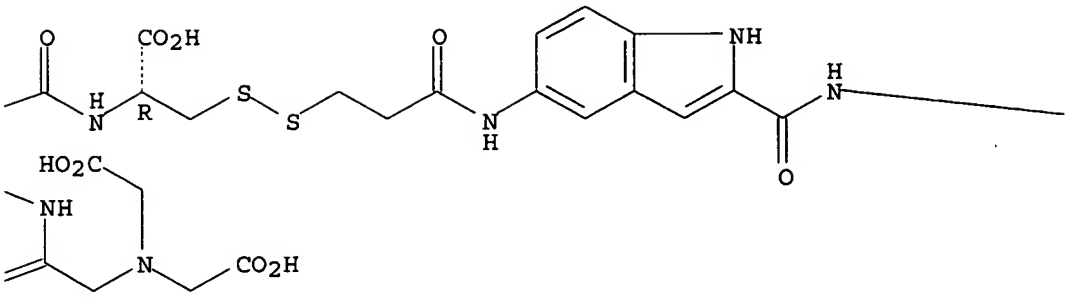

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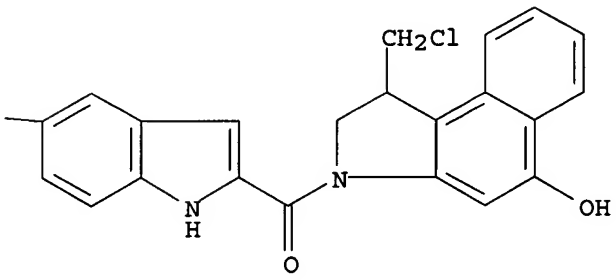

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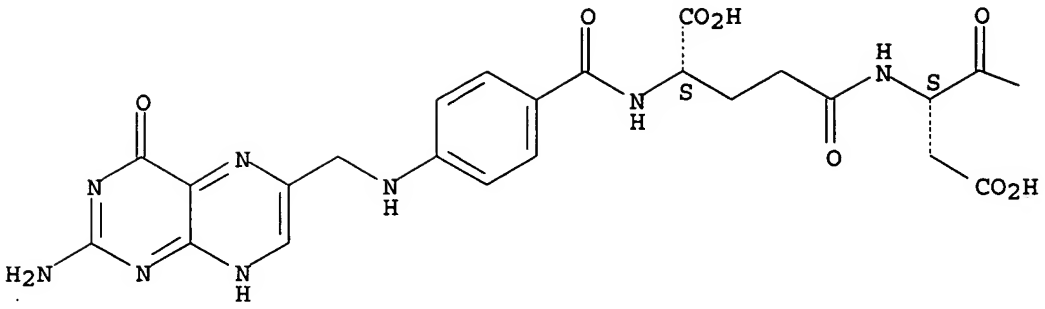
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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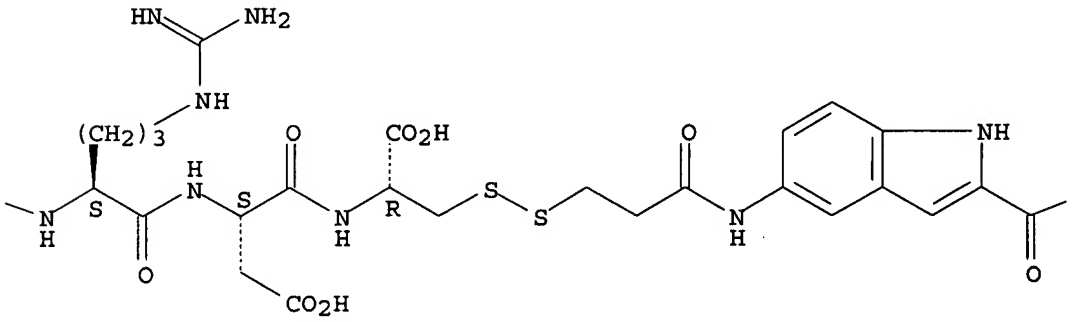

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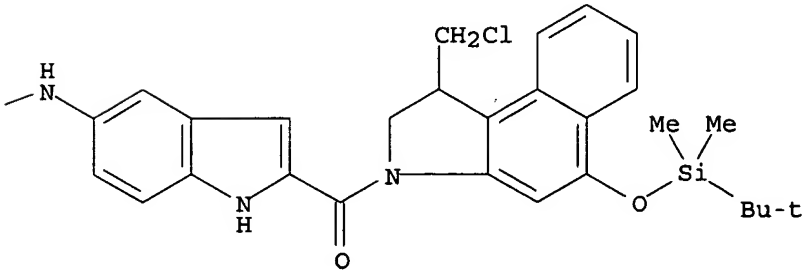

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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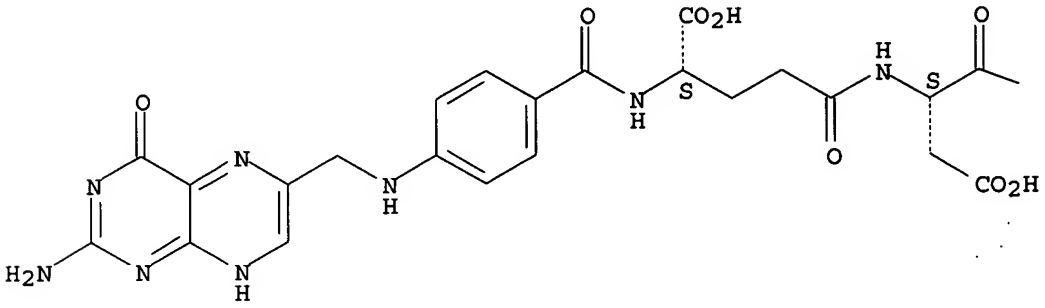
MF C72 H74 Cl N19 O19 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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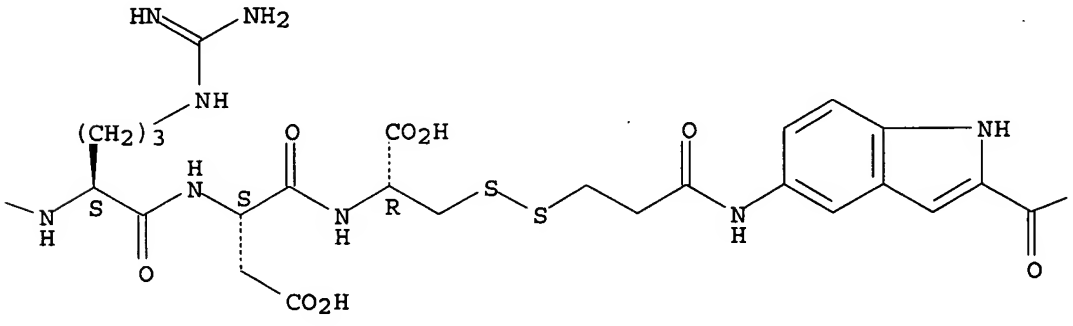

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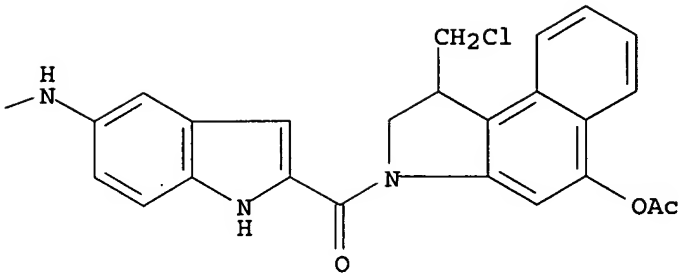

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:207525

L26 ANSWER 10 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 742091-88-9 REGISTRY
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SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
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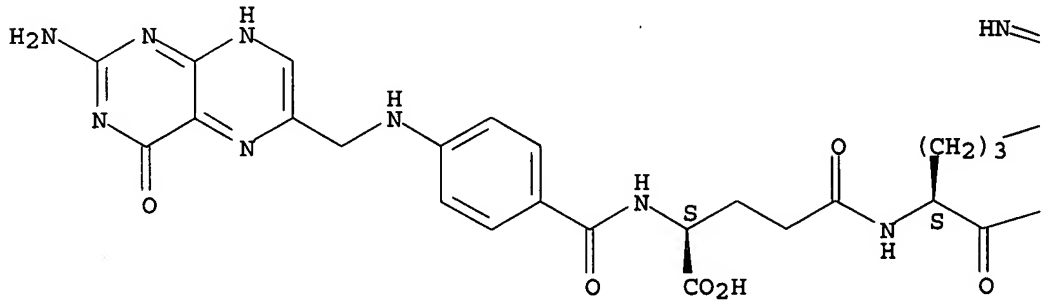
Absolute stereochemistry.

PAGE 1-A



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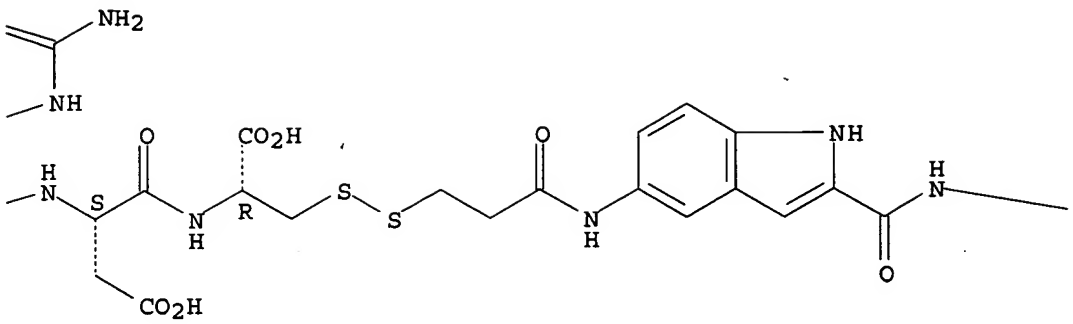

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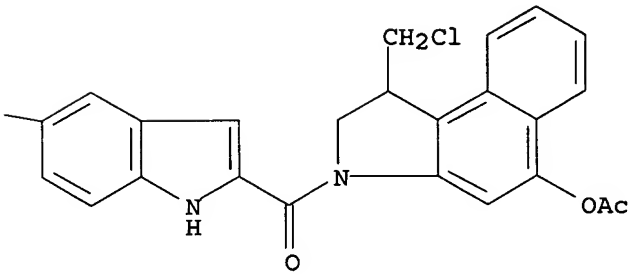

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:207525

L26 ANSWER 11 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
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CN INDEX NAME NOT YET ASSIGNED
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LC STN Files: CA, CAPLUS, TOXCENTER
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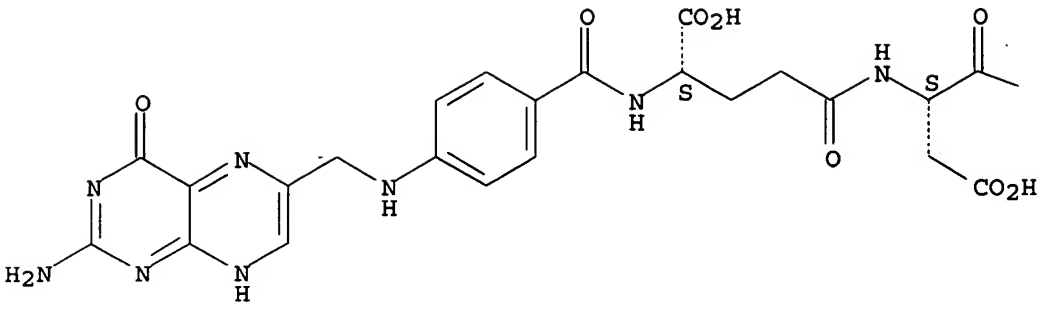
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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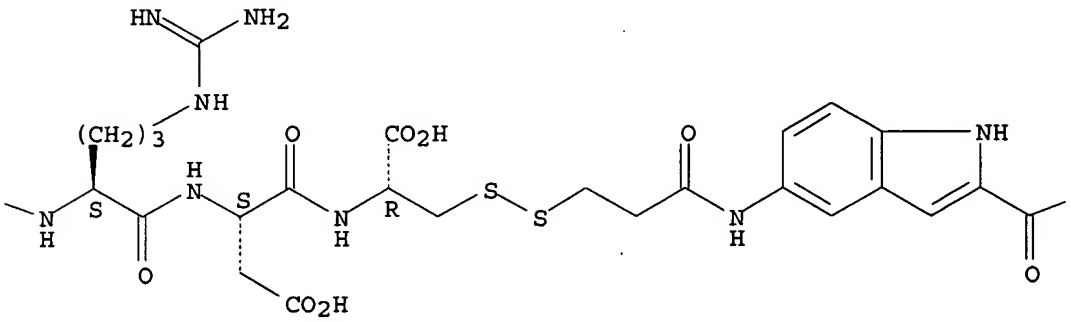

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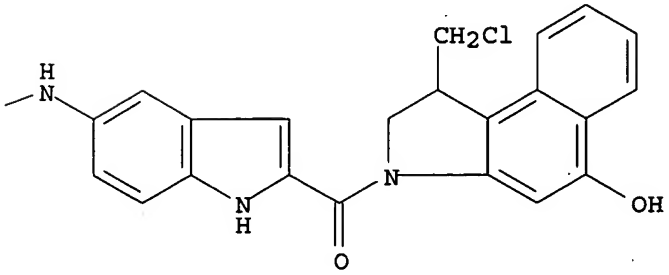

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:207525

L26 ANSWER 12 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 742091-86-7 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
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LC STN Files: CA, CAPLUS, TOXCENTER
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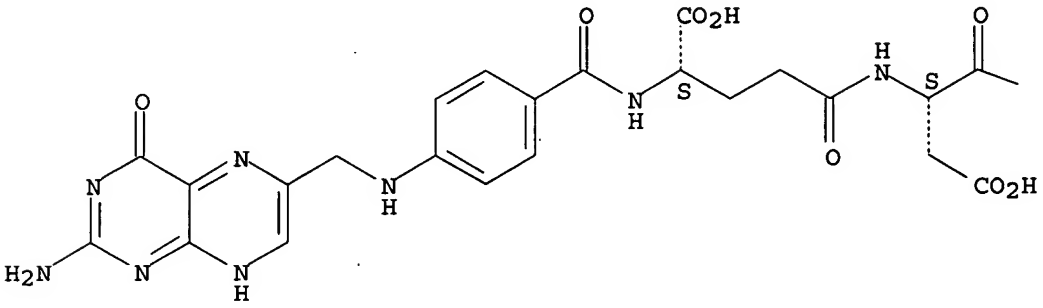
Absolute stereochemistry.

PAGE 1-A



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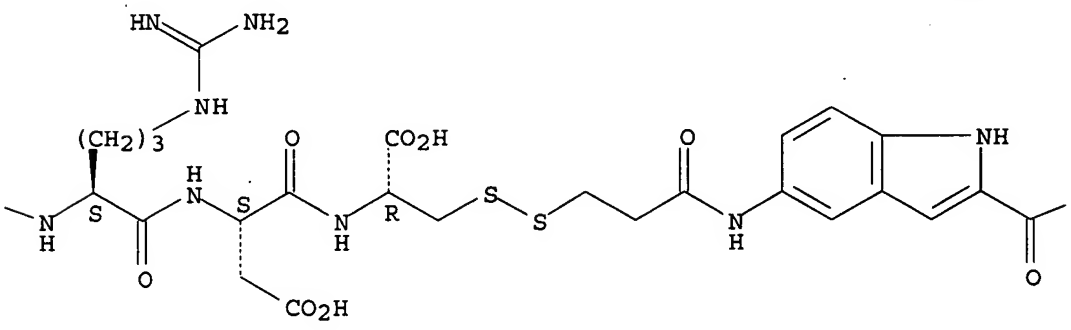

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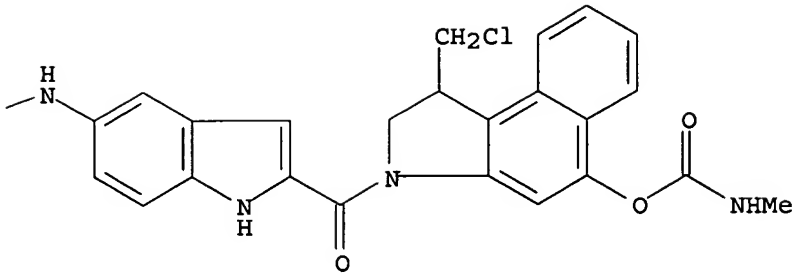

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REFERENCE 1: 141:207525

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FS STEREOSEARCH
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SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
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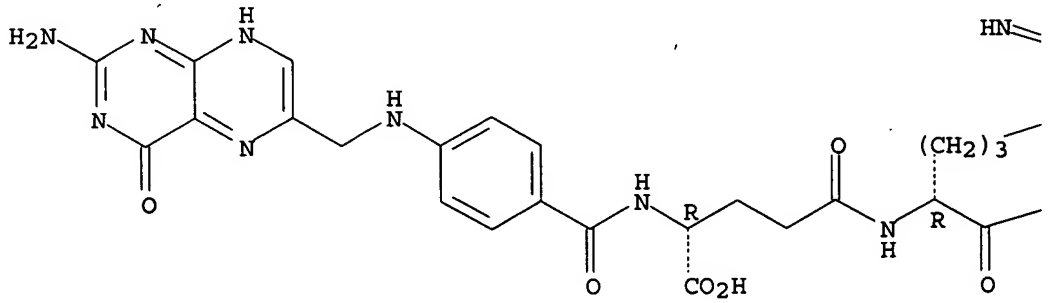
Absolute stereochemistry.

PAGE 1-A



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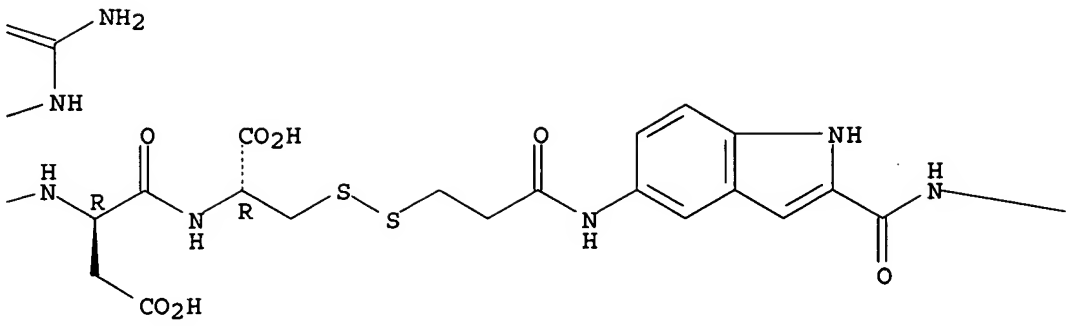

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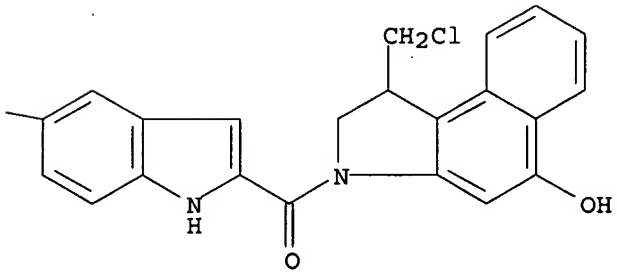

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L26 ANSWER 14 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
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LC STN Files: CA, CAPLUS, TOXCENTER
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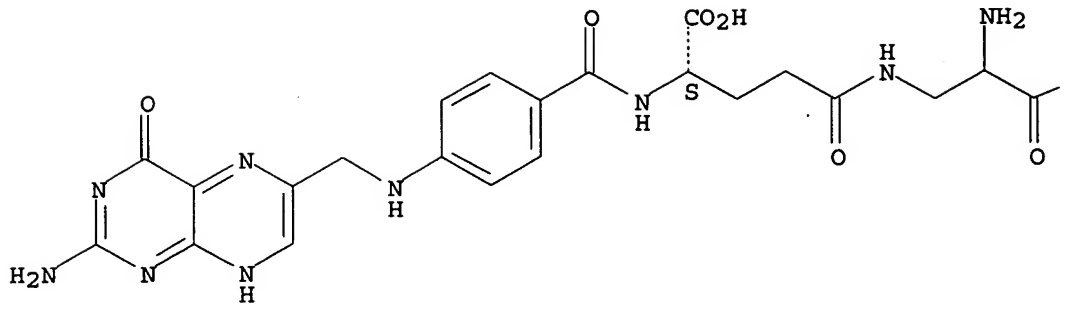
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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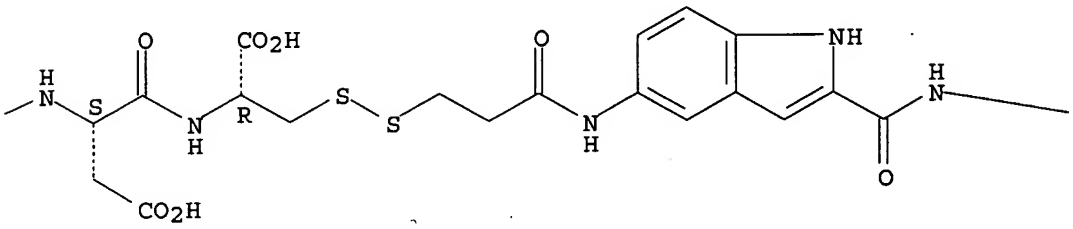

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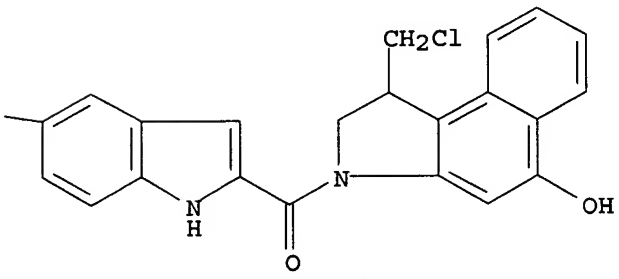

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L26 ANSWER 15 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
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FS STEREOSEARCH
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SR CA

LC STN Files: CA, CAPLUS, TOXCENTER
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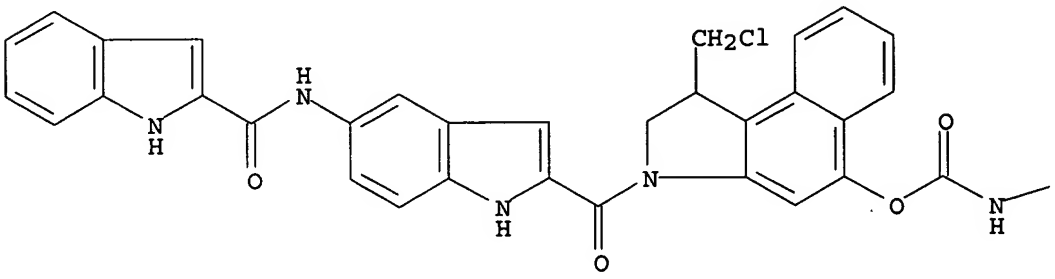
Absolute stereochemistry.

PAGE 1-A



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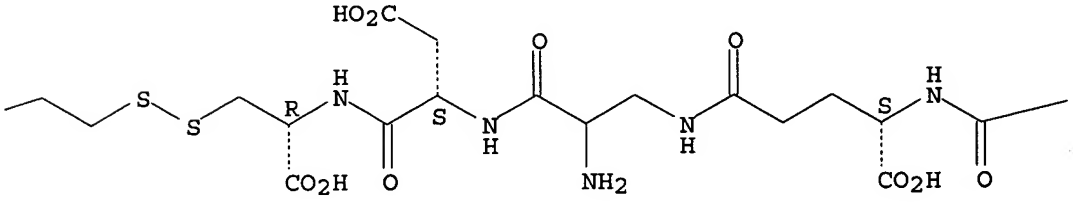

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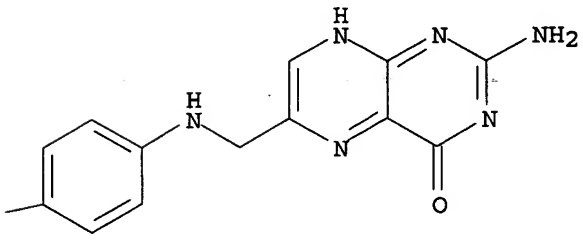

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1 REFERENCES IN FILE CA (1907 TO DATE)
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REFERENCE 1: 141:207525

L26 ANSWER 16 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
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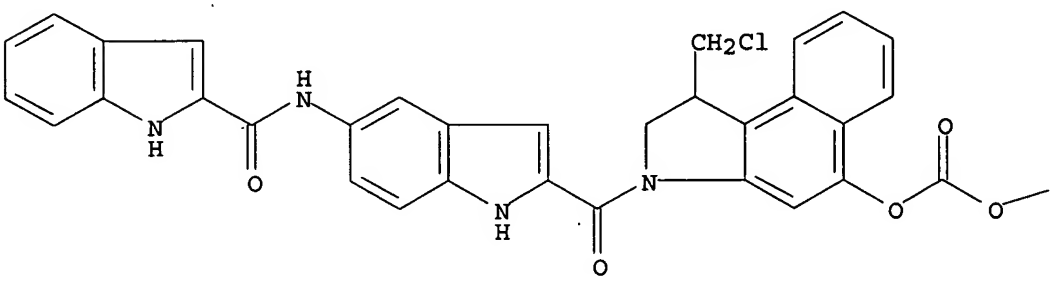
Absolute stereochemistry.

PAGE 1-A



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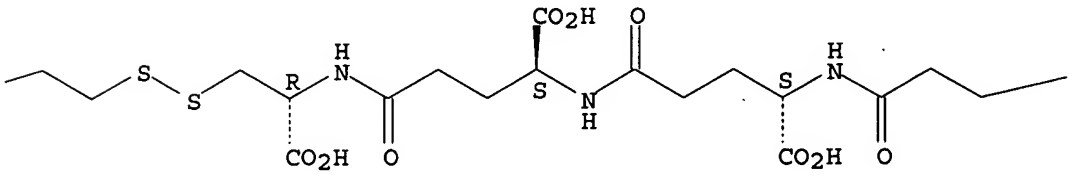

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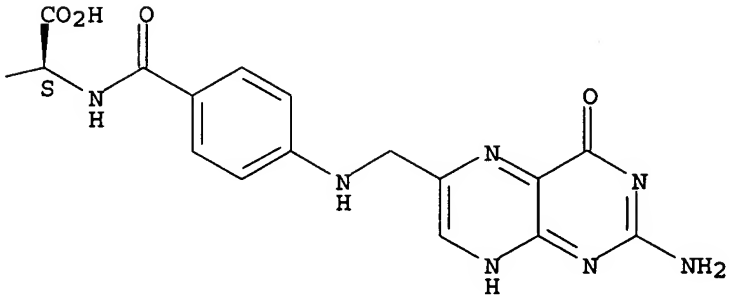

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REFERENCE 1: 141:207525

L26 ANSWER 17 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
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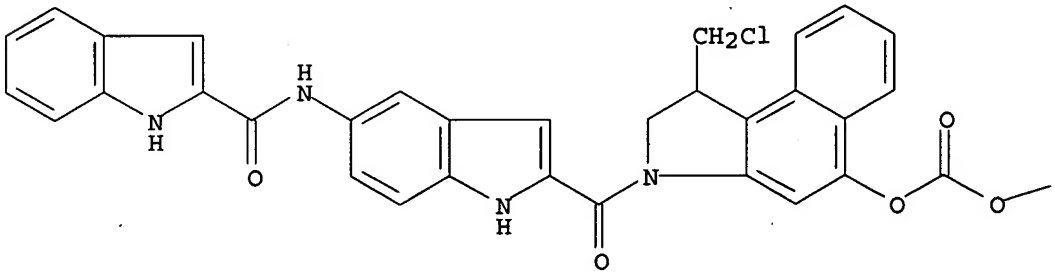
Absolute stereochemistry.

PAGE 1-A



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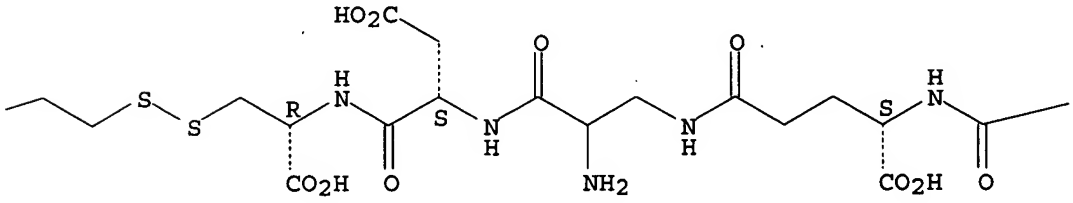

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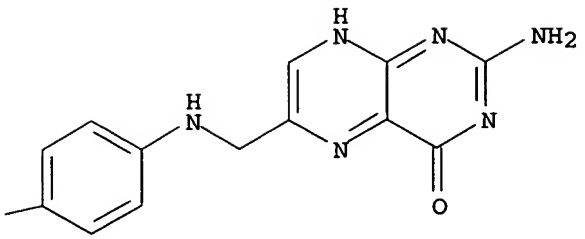

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RN 740842-06-2 REGISTRY
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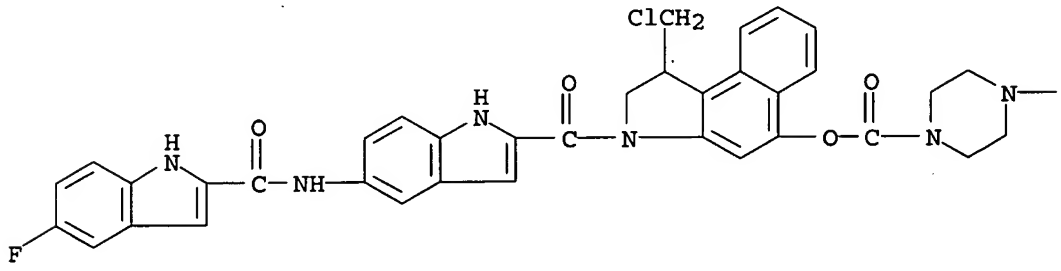
PAGE 1-A



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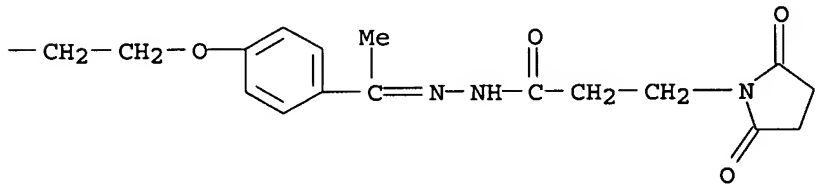

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REFERENCE 1: 141:212819

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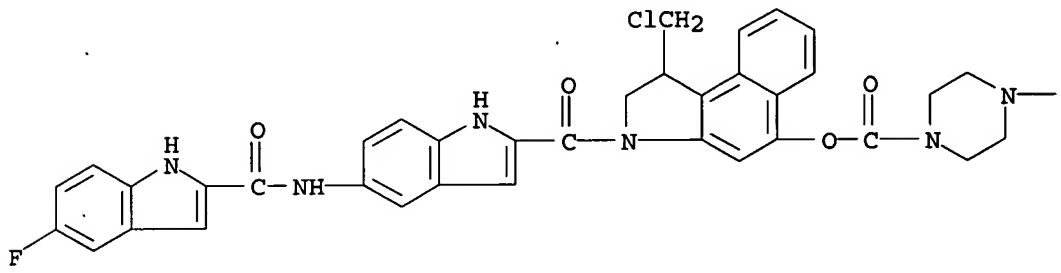
PAGE 1-A



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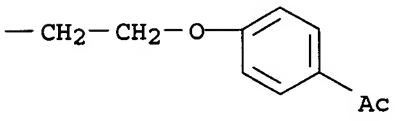

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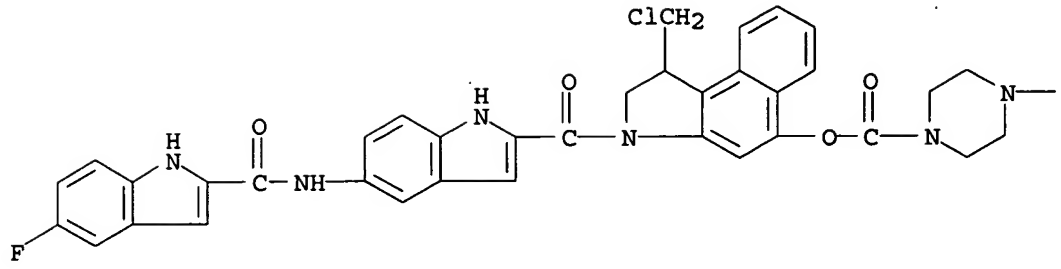
PAGE 1-A



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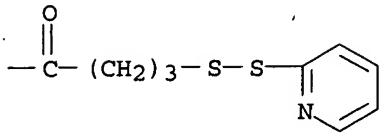

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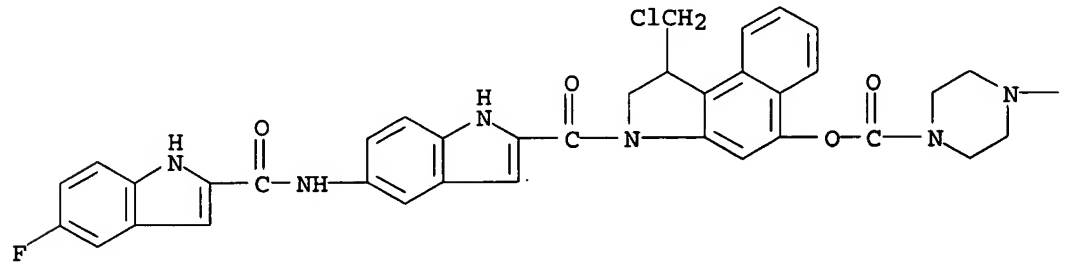
PAGE 1-A



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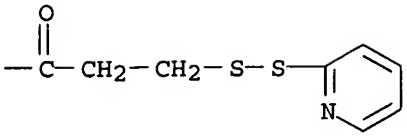

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:212819

L26 ANSWER 22 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 740842-02-8 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
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MF C65 H67 Cl F N7 O5
SR CA
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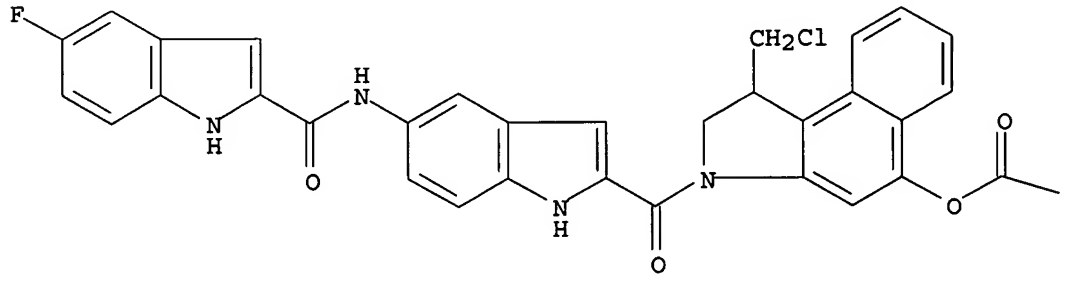
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

Double bond geometry as shown.

PAGE 1-A



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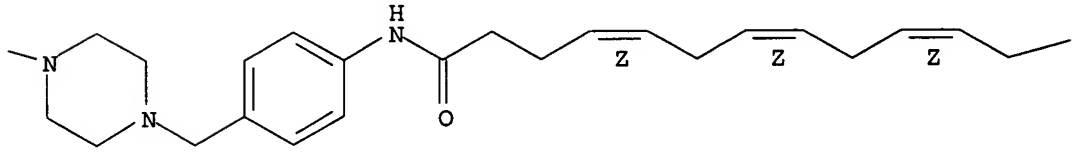

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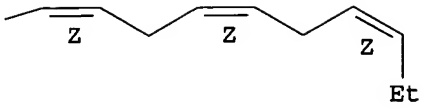

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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:212819

L26 ANSWER 23 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 740842-01-7 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS STEREOSEARCH
MF C53 H52 Cl F N4 O4
SR CA
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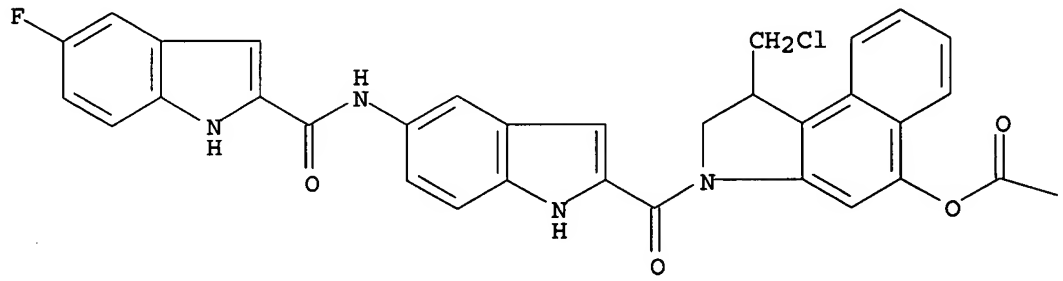
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

Double bond geometry as shown.

PAGE 1-A



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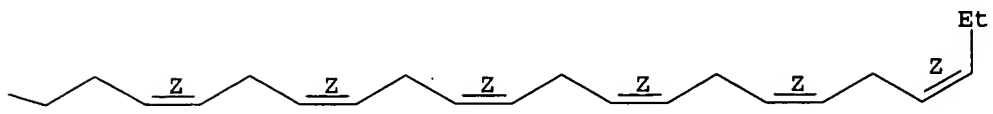

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:212819

L26 ANSWER 24 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 740841-98-9 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
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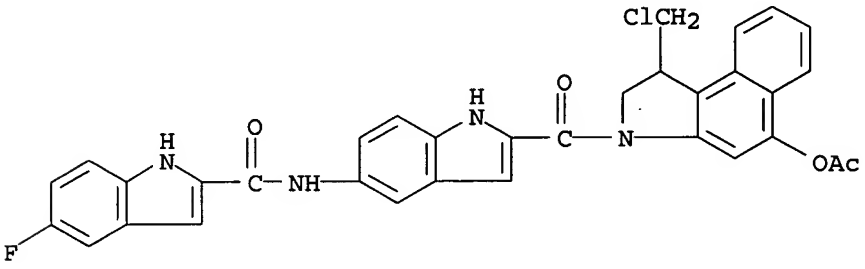
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)



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REFERENCE 1: 141:212819

L26 ANSWER 25 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
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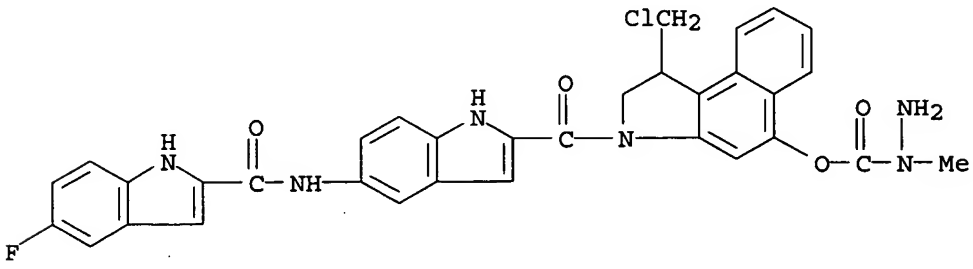

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REFERENCE 1: 141:212819

L26 ANSWER 26 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 740841-96-7 REGISTRY
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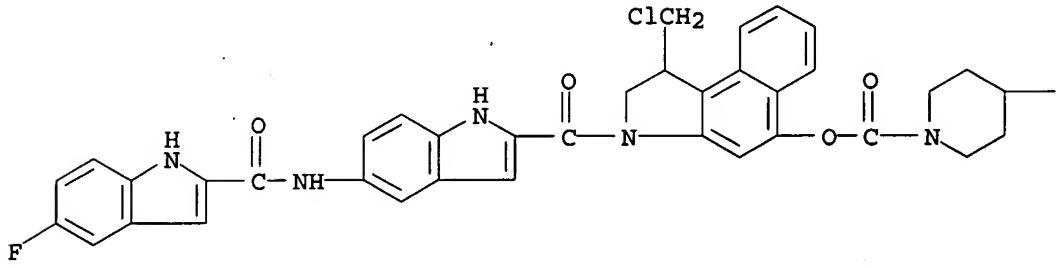
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

PAGE 1-A



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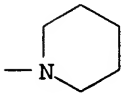

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:212819

L26 ANSWER 27 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 740841-95-6 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
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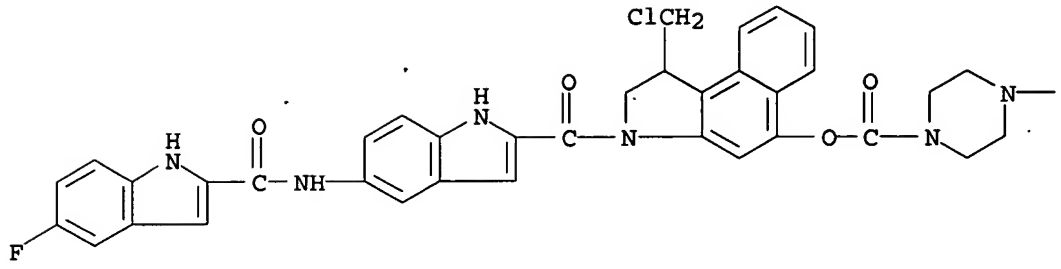
MF C42 H35 Cl F N7 O4
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

PAGE 1-A



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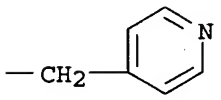

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:212819

L26 ANSWER 28 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 740841-94-5 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
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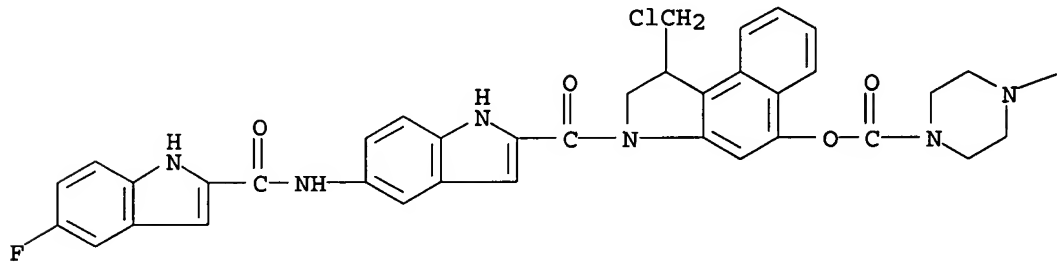
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

PAGE 1-A



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REFERENCE 1: 141:212819

L26 ANSWER 29 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 740841-91-2 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS 3D CONCORD
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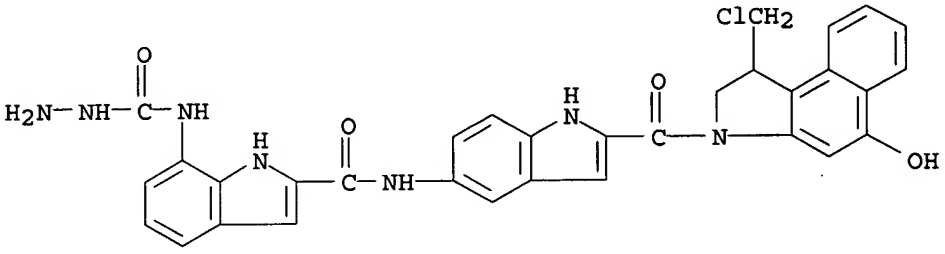
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)



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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:212819

L26 ANSWER 30 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-59-5 REGISTRY
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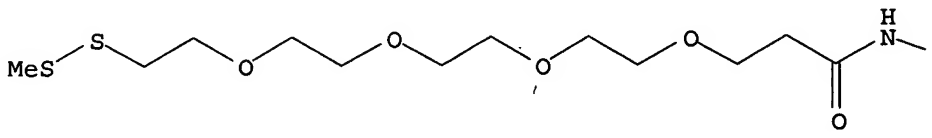
FS STEREOSEARCH
MF C43 H47 Cl N5 O11 P S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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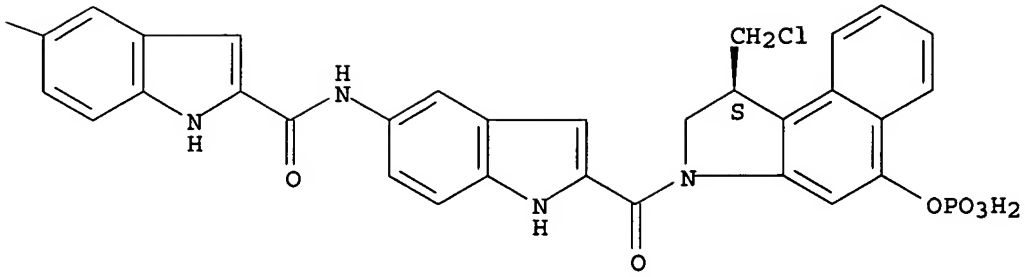

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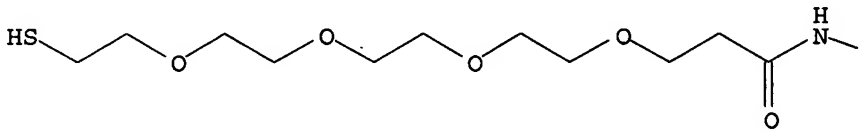
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

L26 ANSWER 31 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-58-4 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-(phosphonooxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(15-mercapto-1-oxo-4,7,10,13-tetraoxapentadec-1-yl)amino]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C42 H45 Cl N5 O11 P S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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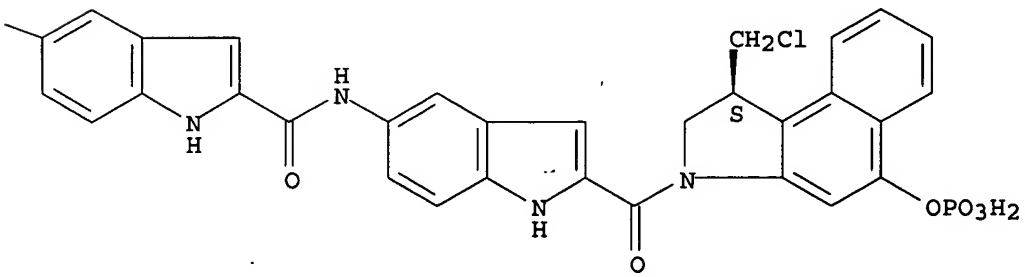

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

L26 ANSWER 32 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-57-3 REGISTRY
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FS STEREOSEARCH
MF C54 H64 Cl N7 O9 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
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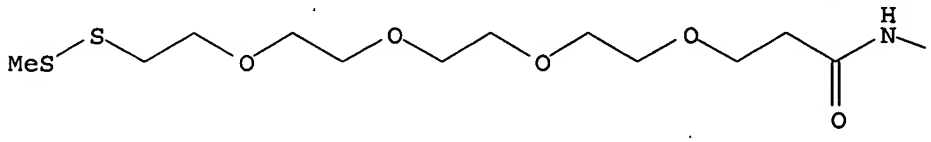
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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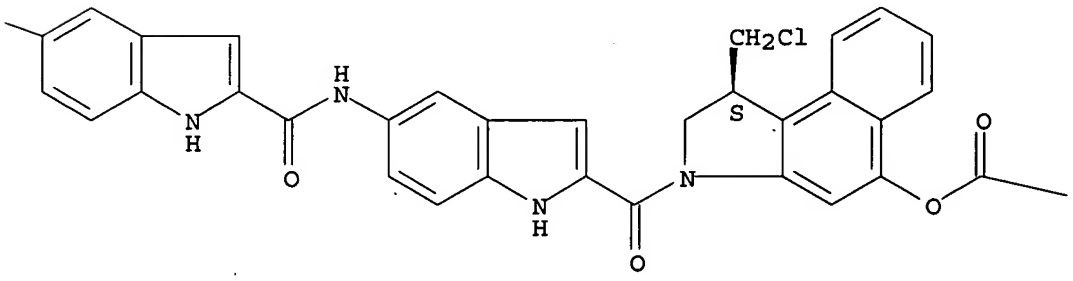

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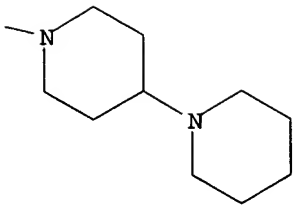

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

L26 ANSWER 33 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-56-2 REGISTRY
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[5-[[[5-[(15-mercapto-1-oxo-4,7,10,13-tetraoxapentadec-1-yl)amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C53 H62 Cl N7 O9 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
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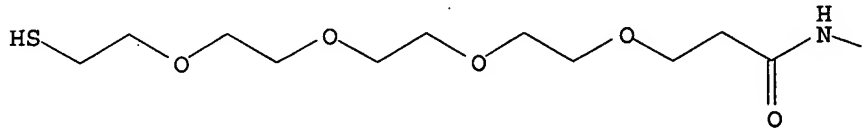
Absolute stereochemistry.

PAGE 1-A



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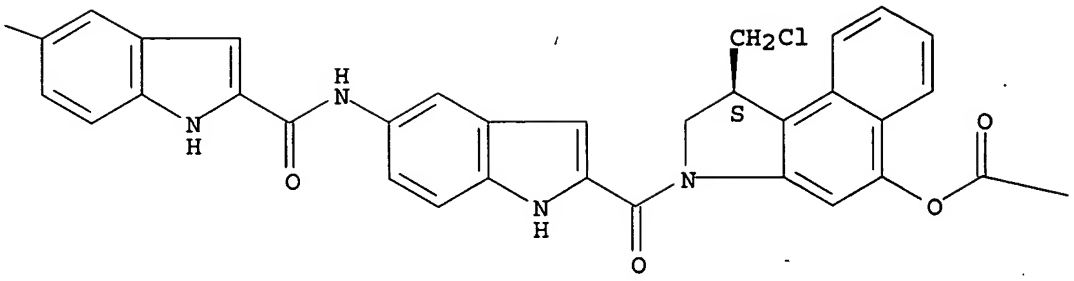

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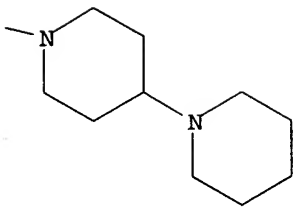

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

L26 ANSWER 34 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-55-1 REGISTRY
CN 1-Piperazinecarboxylic acid, 4-methyl-, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[5-[[[5-[(1-oxo-4,7,10,13-tetraoxa-16,17-dithiaoctadec-1-yl)amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C49 H56 Cl N7 O9 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
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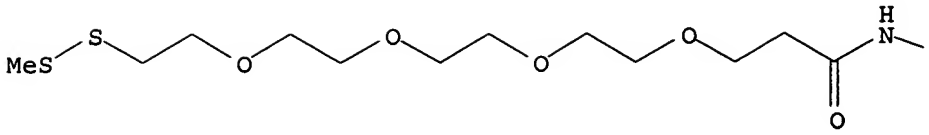
Absolute stereochemistry.

PAGE 1-A



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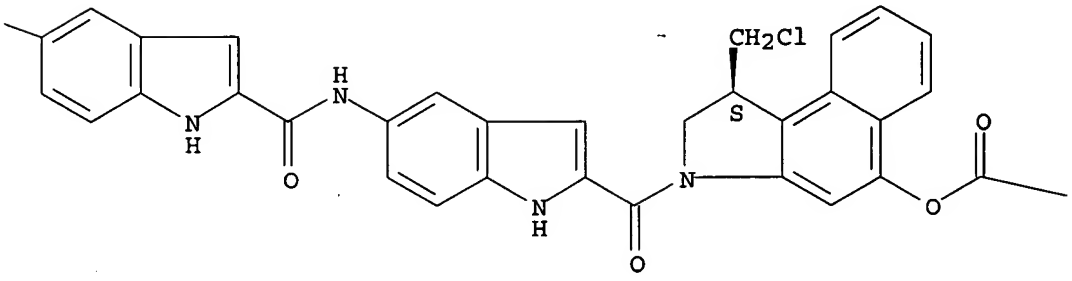

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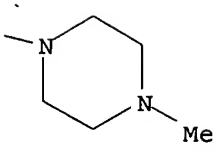

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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

L26 ANSWER 35 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-54-0 REGISTRY
CN 1-Piperazinecarboxylic acid, 4-methyl-, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[5-[[[5-[(15-mercapto-1-oxo-4,7,10,13-tetraoxapentadec-1-yl)amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C48 H54 Cl N7 O9 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
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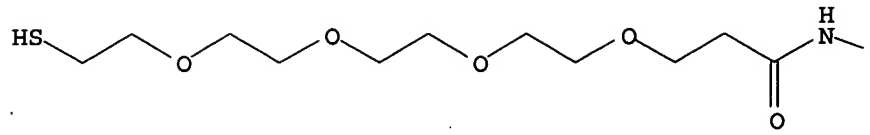
Absolute stereochemistry.

PAGE 1-A



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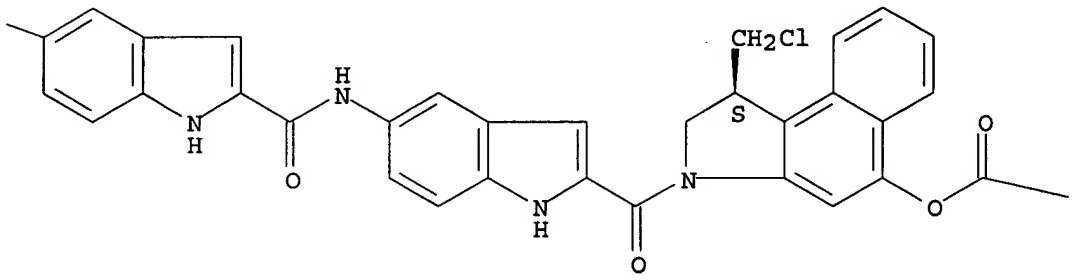
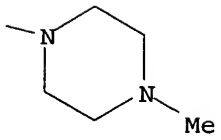


PAGE 1-C



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

L26 ANSWER 36 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-53-9 REGISTRY
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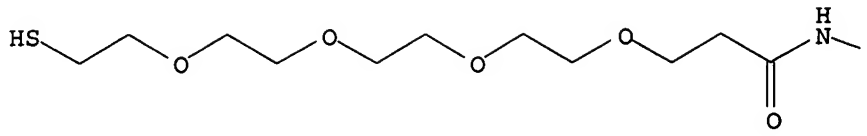
FS STEREOSEARCH
MF C42 H44 Cl N5 O8 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES

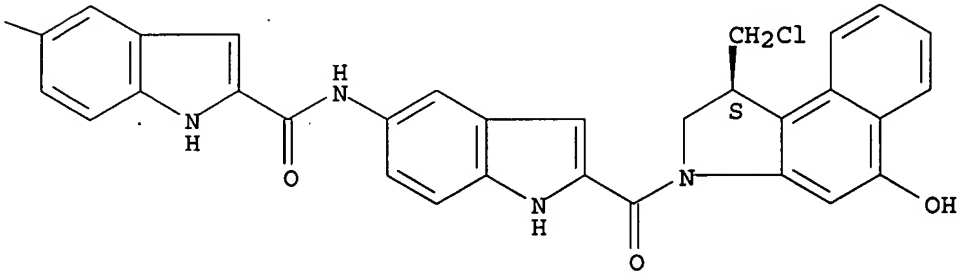
(Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

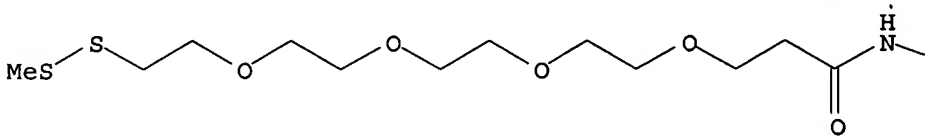
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

L26 ANSWER 37 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-52-8 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(1-oxo-4,7,10,13-tetraoxa-16,17-dithiaoctadec-1-yl)amino]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C43 H46 Cl N5 O8 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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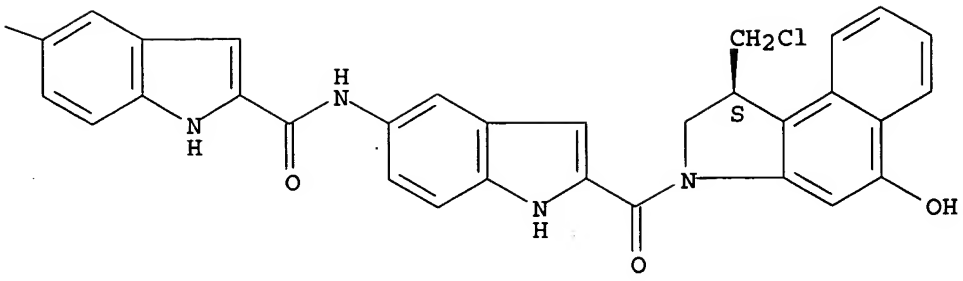
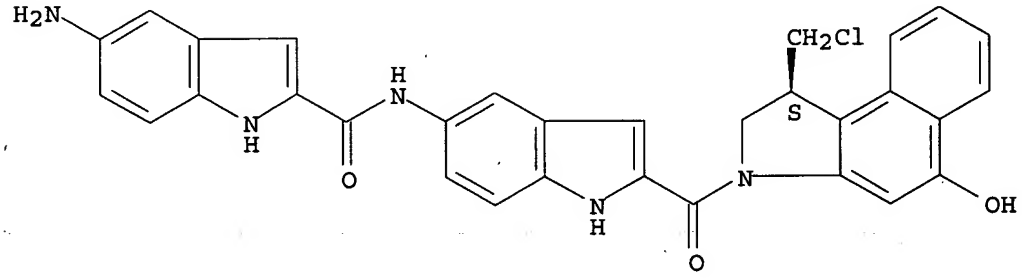


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

L26 ANSWER 38 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-51-7 REGISTRY
CN 1H-Indole-2-carboxamide, 5-amino-N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H24 Cl N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

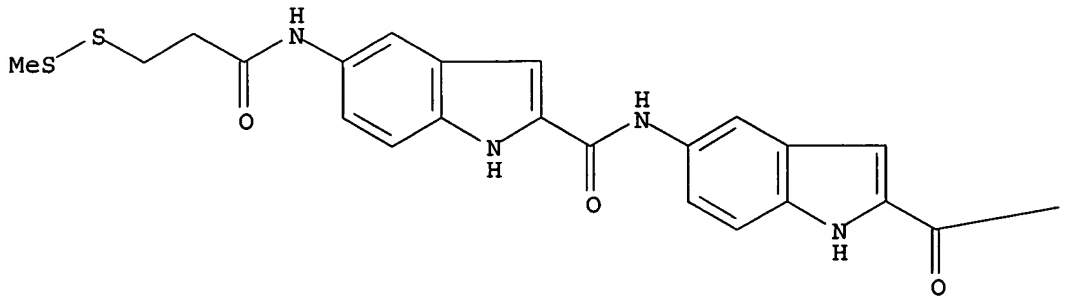
REFERENCE 1: 139:341741

L26 ANSWER 39 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-49-3 REGISTRY
CN Phosphoric acid, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[5-[[[5-[[3-(methyldithio)-1-oxopropyl]amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl bis(phenylmethyl) ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C49 H43 Cl N5 O7 P S2

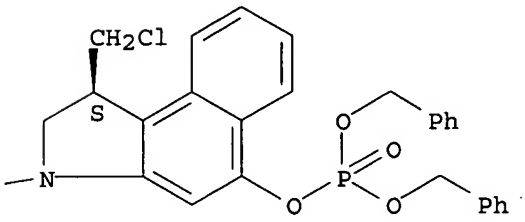
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

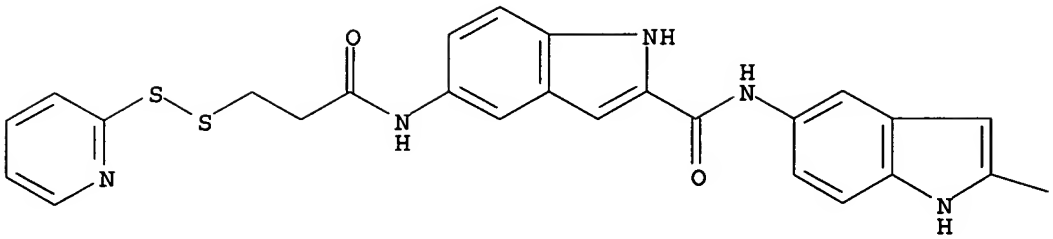
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

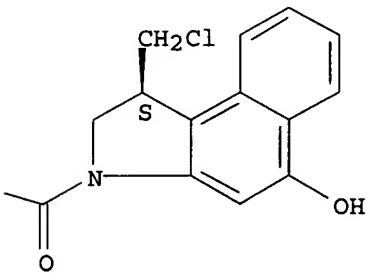
L26 ANSWER 40 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 501666-87-1 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[[1-oxo-3-(2-pyridinyldithio)propyl]amino]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C39 H31 Cl N6 O4 S2
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



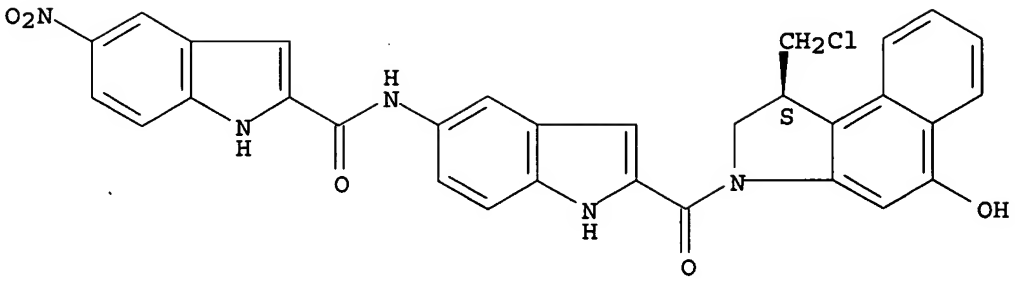
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:238007

L26 ANSWER 41 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 501441-05-0 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole
FS STEREOSEARCH
MF C31 H22 Cl N5 O5
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.



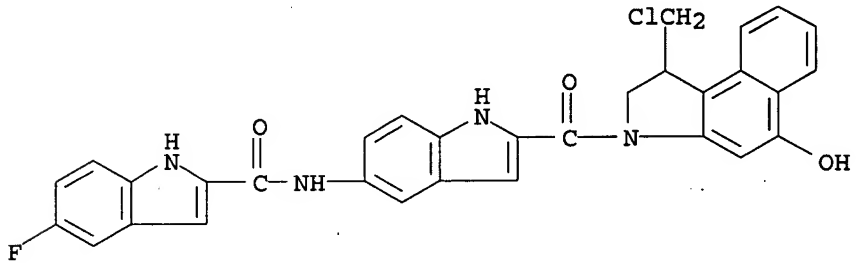
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

REFERENCE 2: 138:238007

L26 ANSWER 42 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 500536-51-6 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-fluoro- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C31 H22 Cl F N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

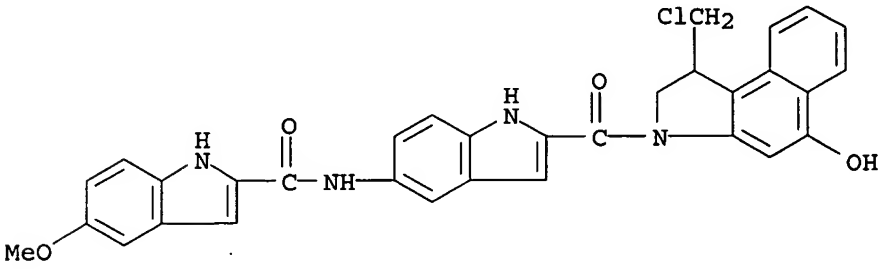
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:212819

REFERENCE 2: 138:204856

L26 ANSWER 43 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 500536-49-2 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-methoxy- (9CI) (CA INDEX NAME)

FS 3D CONCORD
MF C32 H25 Cl N4 O4
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

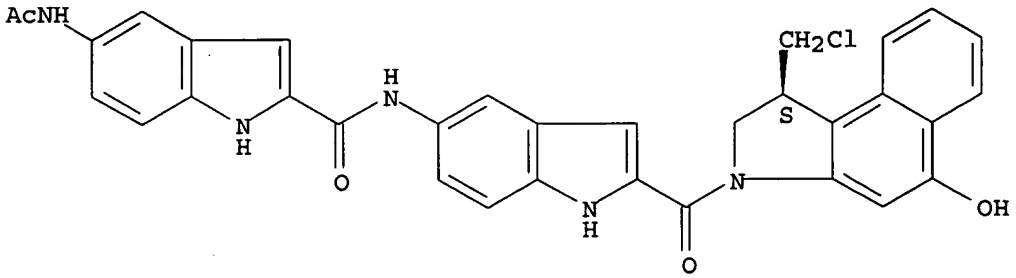
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:212819

REFERENCE 2: 138:204856

L26 ANSWER 44 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 500536-47-0 REGISTRY
CN 1H-Indole-2-carboxamide, 5-(acetylamino)-N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H26 Cl N5 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).



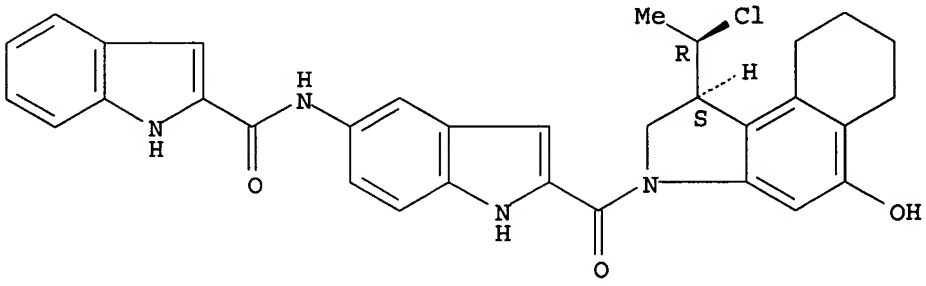
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:204856

L26 ANSWER 45 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 452921-80-1 REGISTRY

CN 1H-Indole-2-carboxamide, N-[2-[[(1R)-1-[(1S)-1-chloroethyl]-1,2,6,7,8,9-hexahydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H29 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Relative stereochemistry.



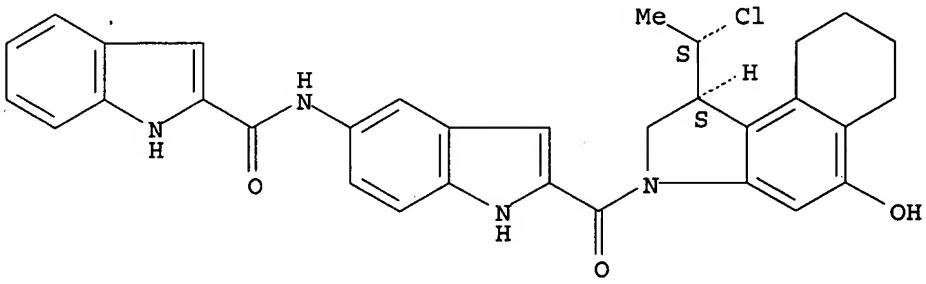
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:201172

L26 ANSWER 46 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 452921-79-8 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1R)-1-[(1R)-1-chloroethyl]-1,2,6,7,8,9-hexahydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H29 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Relative stereochemistry.

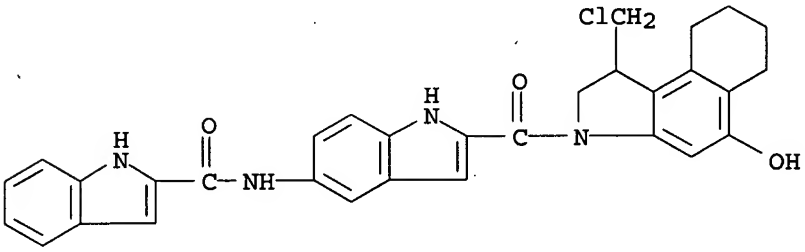


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:201172

L26 ANSWER 47 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 452921-78-7 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2,6,7,8,9-hexahydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C31 H27 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



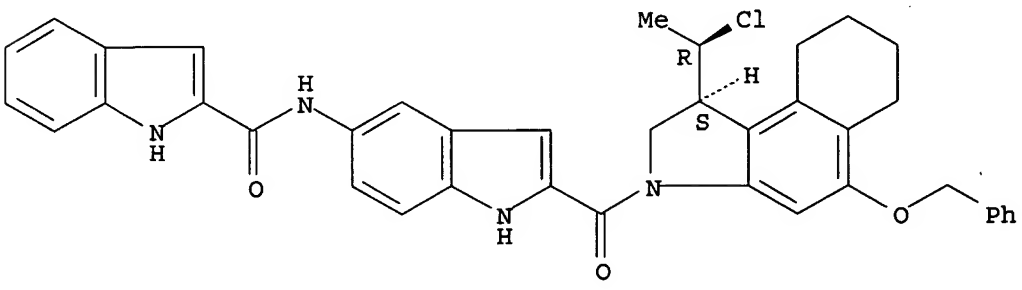
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:201172

L26 ANSWER 48 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 452921-77-6 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1R)-1-[(1S)-1-chloroethyl]-1,2,6,7,8,9-hexahydro-5-(phenylmethoxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C39 H35 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Relative stereochemistry.



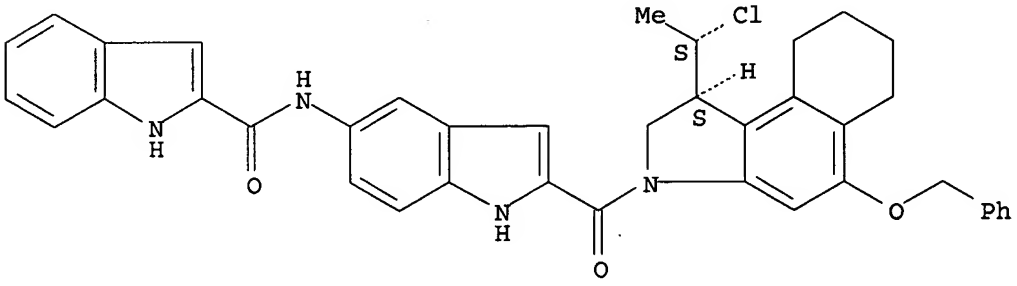
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:201172

L26 ANSWER 49 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 452921-76-5 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1R)-1-[(1R)-1-chloroethyl]-1,2,6,7,8,9-hexahydro-5-(phenylmethoxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C39 H35 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Relative stereochemistry.

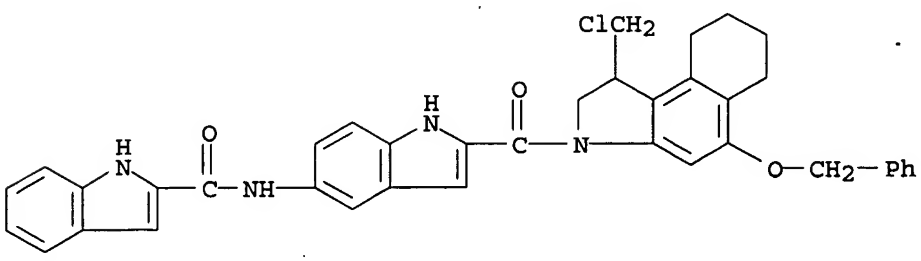


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:201172

L26 ANSWER 50 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 452921-75-4 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2,6,7,8,9-hexahydro-5-(phenylmethoxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C38 H33 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

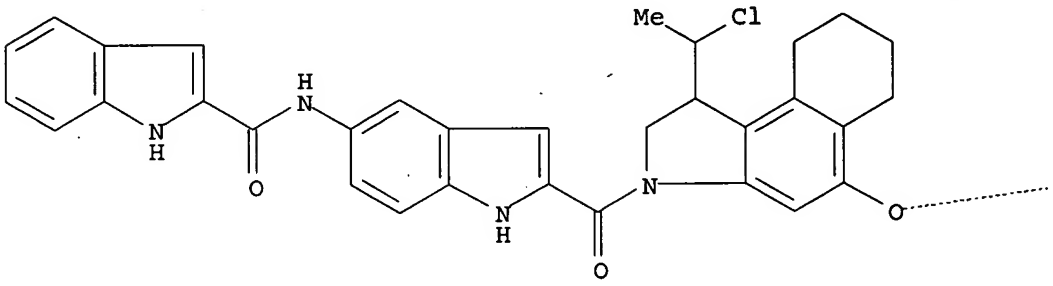
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:201172

L26 ANSWER 51 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 452921-66-3 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(1-chloroethyl)-5-(β-D-galactopyranosyloxy)-1,2,6,7,8,9-hexahydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H39 Cl N4 O8
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry.

PAGE 1-A



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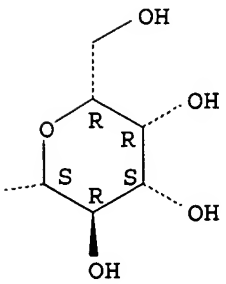


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

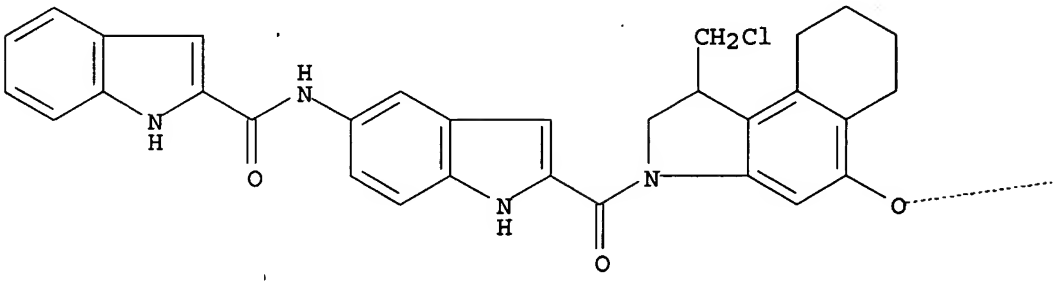
REFERENCE 1: 137:201172

L26 ANSWER 52 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 452921-65-2 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-5-(β-D-galactopyranosyloxy)-1,2,6,7,8,9-hexahydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

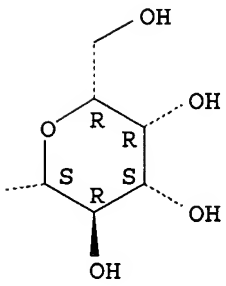
FS STEREOSEARCH
MF C37 H37 Cl N4 O8
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



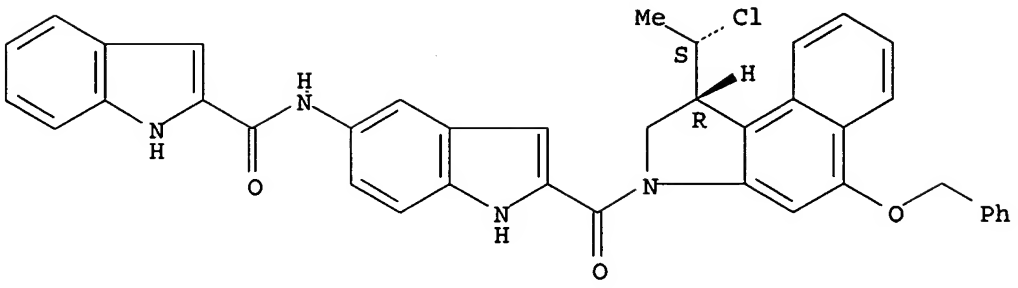
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:201172

L26 ANSWER 53 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390362-73-9 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1R)-1-[(1S)-1-chloroethyl]-1,2-dihydro-5-(phenylmethoxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C39 H31 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.



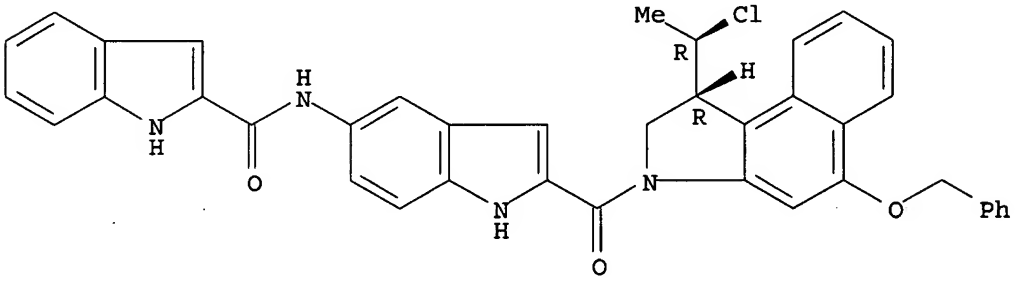
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:112208

L26 ANSWER 54 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390362-72-8 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1R)-1-[(1R)-1-chloroethyl]-1,2-dihydro-5-(phenylmethoxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C39 H31 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

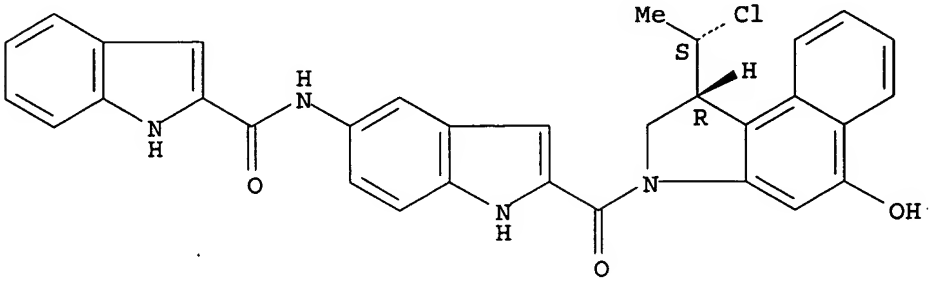
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:112208

L26 ANSWER 55 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390362-71-7 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1R)-1-[(1S)-1-chloroethyl]-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H25 Cl N4 O3

SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.



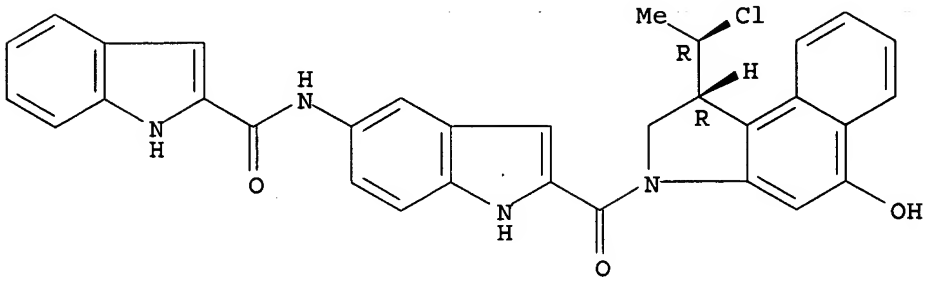
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:112208

L26 ANSWER 56 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390362-70-6 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1R)-1-[(1R)-1-chloroethyl]-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H25 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

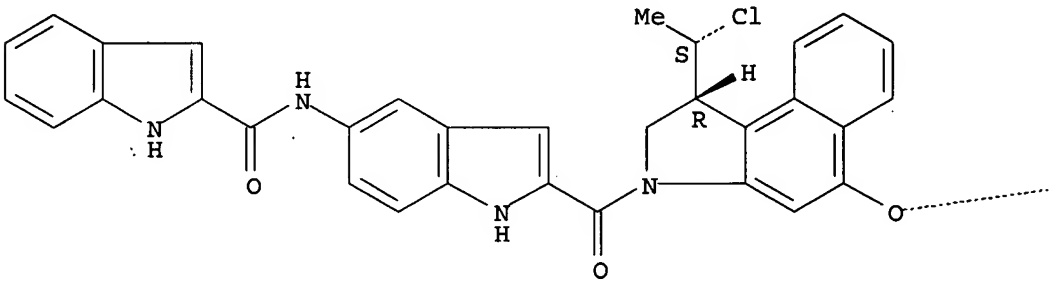
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:112208

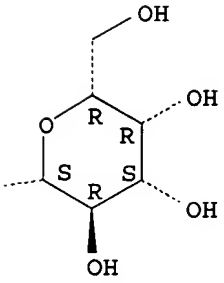
L26 ANSWER 57 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390362-69-3 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1R)-1-[(1S)-1-chloroethyl]-5-(β-D-galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H35 Cl N4 O8
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

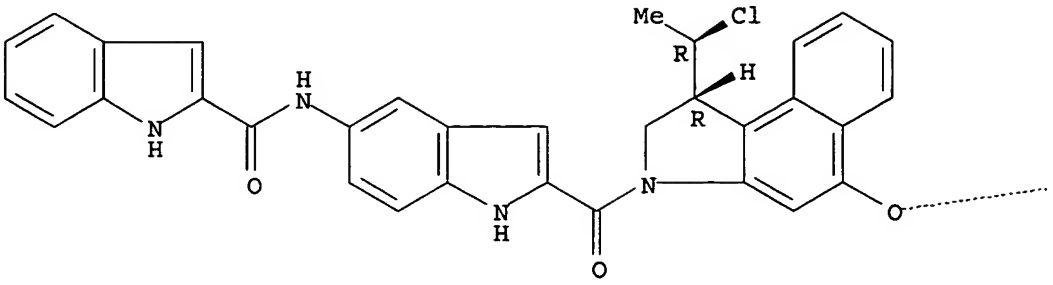
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:112208

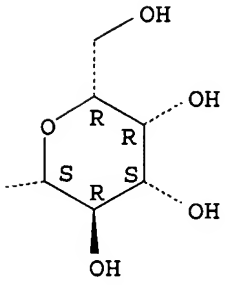
L26 ANSWER 58 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390362-68-2 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1R)-1-[(1R)-1-chloroethyl]-5-(β-D-galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H35 Cl N4 O8
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

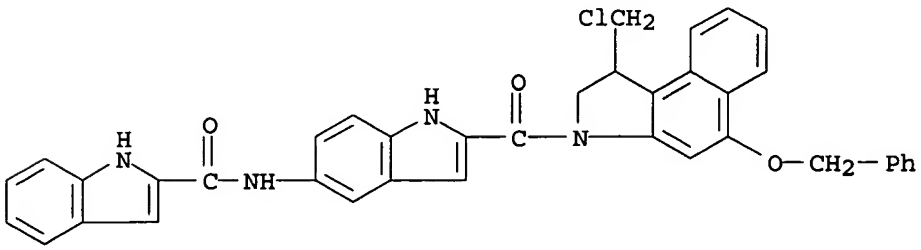


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:112208

L26 ANSWER 59 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390362-64-8 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-(phenylmethoxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C38 H29 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

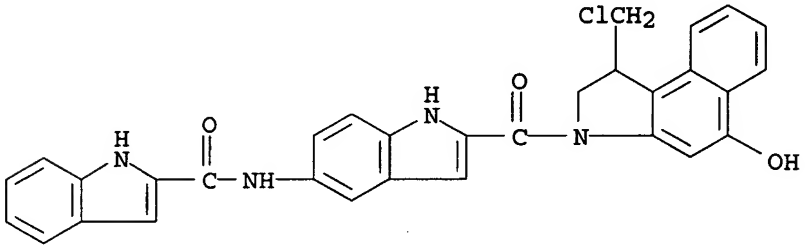


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:112208

L26 ANSWER 60 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390362-63-7 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C31 H23 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

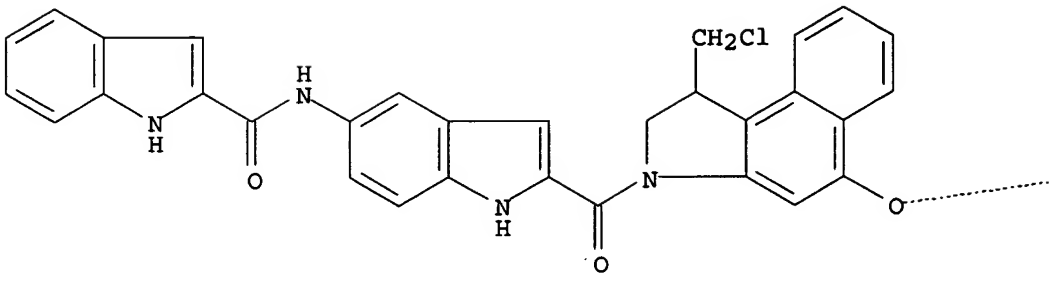
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:112208

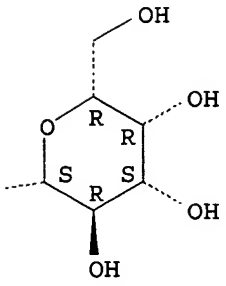
L26 ANSWER 61 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390362-62-6 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-5-(β-D-galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C37 H33 Cl N4 O8
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

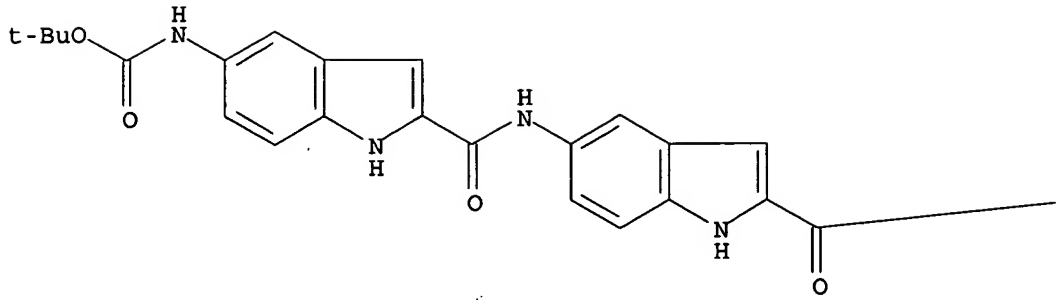
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:112208

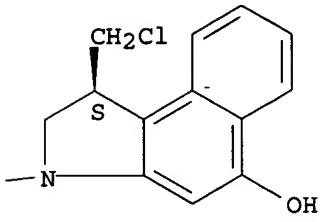
L26 ANSWER 62 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 372954-24-0 REGISTRY
CN Carbamic acid, [2-[[[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C36 H32 Cl N5 O5
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

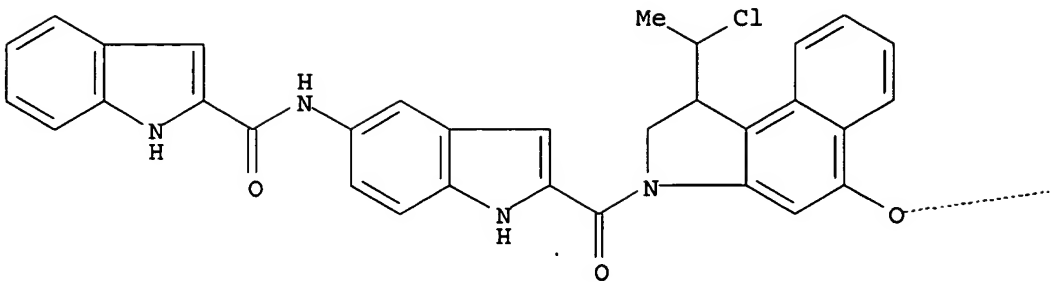
REFERENCE 1: 138:255007

REFERENCE 2: 135:357786

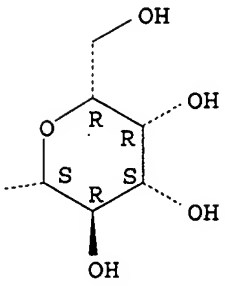
L26 ANSWER 63 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 330206-90-1 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(1-chloroethyl)-5-(β-D-galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H35 Cl N4 O8
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

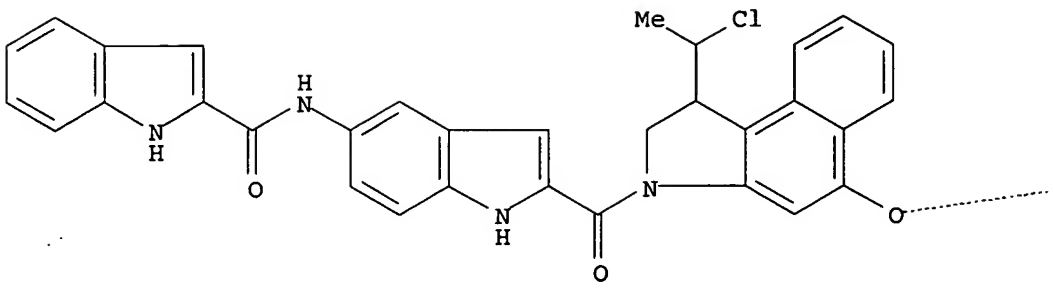
REFERENCE 1: 135:344672

REFERENCE 2: 134:237751

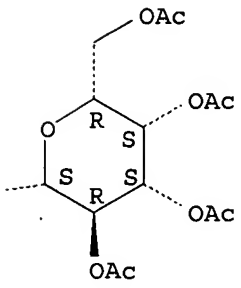
L26 ANSWER 64 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 330206-89-8 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(1-chloroethyl)-1,2-dihydro-5-[(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)oxy]-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C46 H43 Cl N4 O12
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

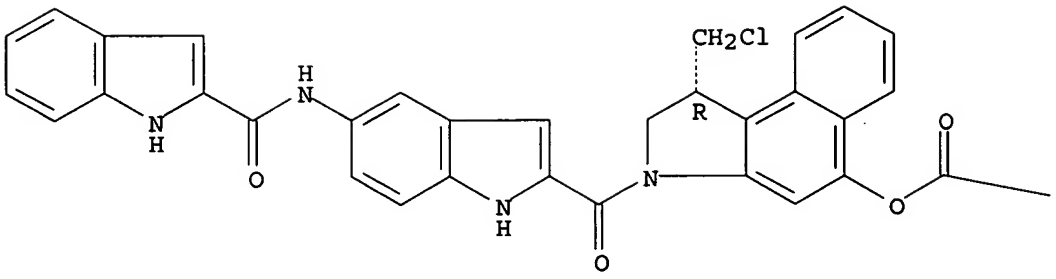
REFERENCE 1: 135:344672

REFERENCE 2: 134:237751

L26 ANSWER 65 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 244154-68-5 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1R)-1-(chloromethyl)-1,2-dihydro-5-[[(phenylamino)carbonyl]oxy]-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H28 Cl N5 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

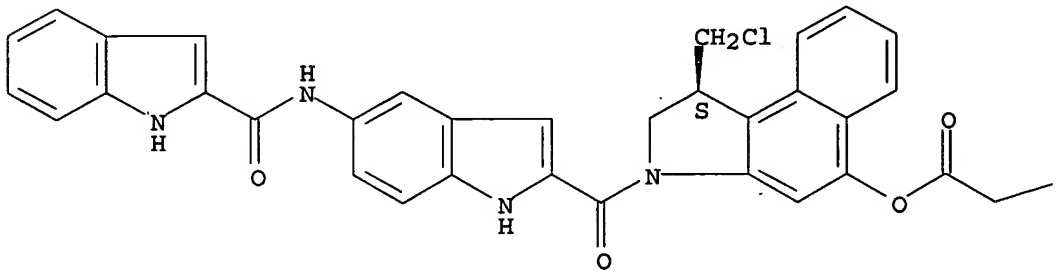
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:237670

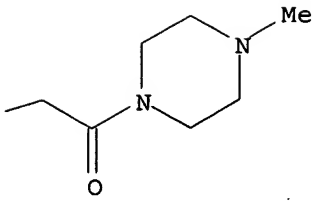
L26 ANSWER 66 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 244154-65-2 REGISTRY
CN 1-Piperazinebutanoic acid, 4-methyl-γ-oxo-, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C40 H37 Cl N6 O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B



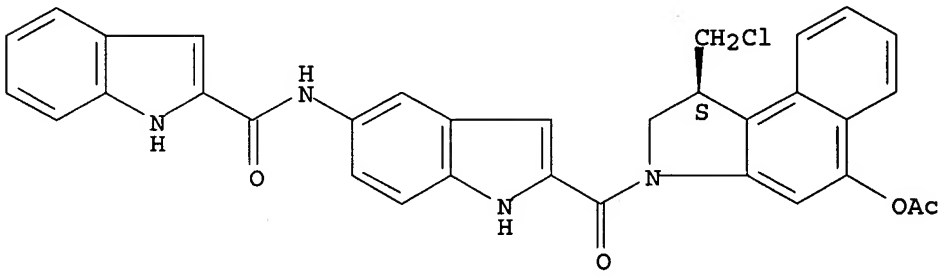
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:237670

L26 ANSWER 67 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 244154-64-1 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-5-(acetyloxy)-1-(chloromethyl)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H25 Cl N4 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

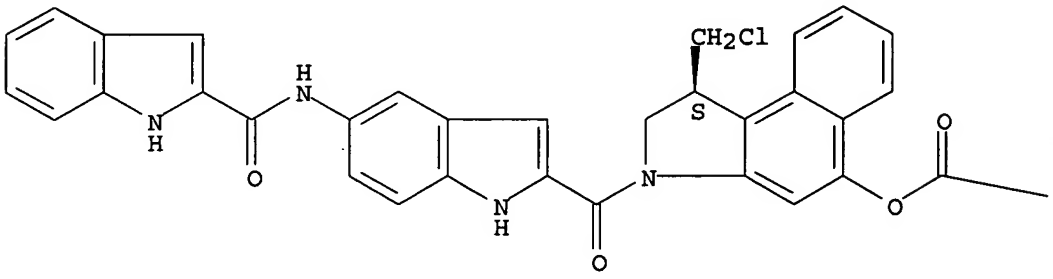
REFERENCE 1: 131:237670

L26 ANSWER 68 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 244154-63-0 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-[[(methylamino)carbonyl]oxy]-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H26 Cl N5 O4

SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

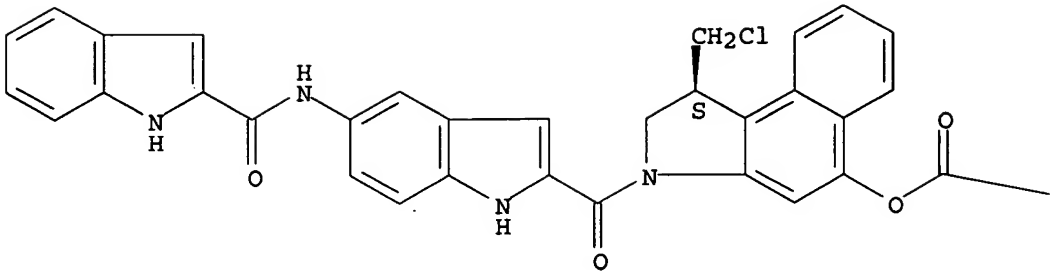
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:237670

L26 ANSWER 69 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 244154-62-9 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-[[(phenylamino)carbonyl]oxy]-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H28 Cl N5 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

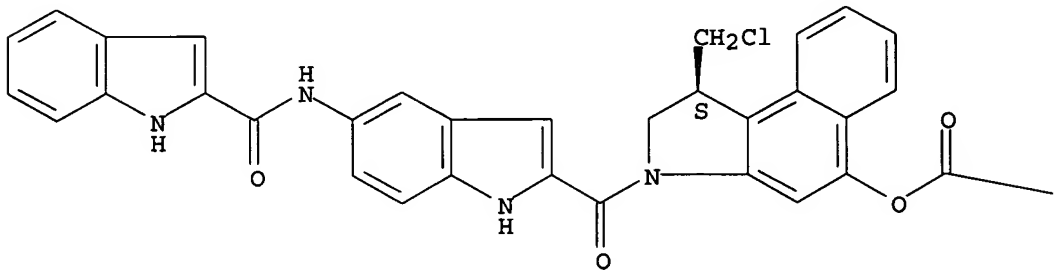
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:237670

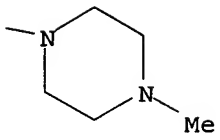
L26 ANSWER 70 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 244154-61-8 REGISTRY
CN 1-Piperazinecarboxylic acid, 4-methyl-, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C37 H33 Cl N6 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

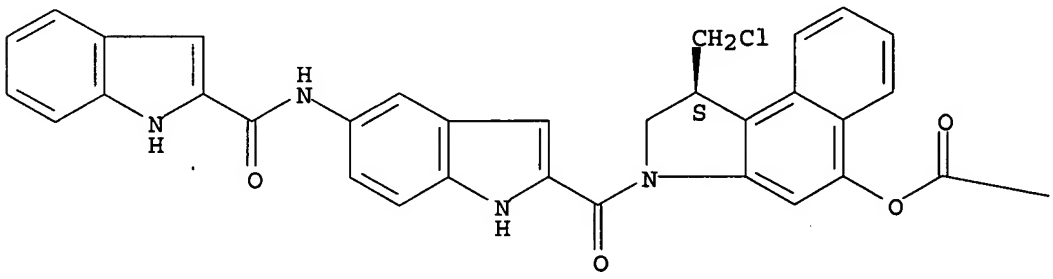
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:237670

L26 ANSWER 71 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 244154-60-7 REGISTRY
CN Carbamic acid, dimethyl-, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H28 Cl N5 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

—NMe2

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

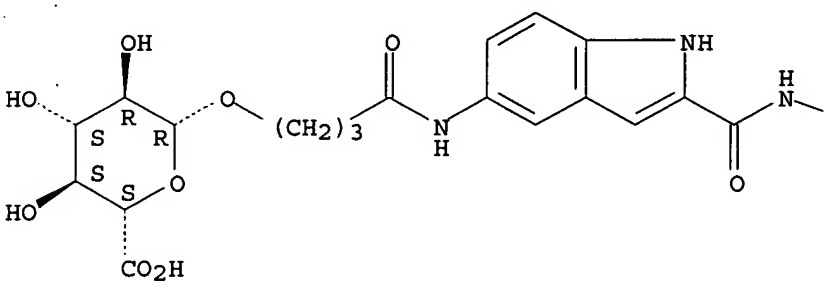
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:237670

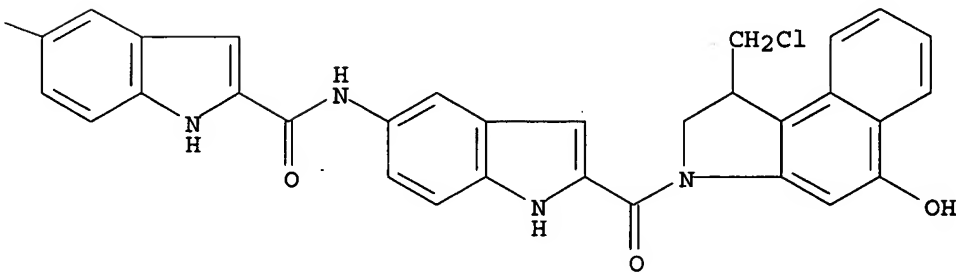
L26 ANSWER 72 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 199806-65-0 REGISTRY
CN β-D-Glucopyranosiduronic acid, 4-[[2-[[[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]-4-oxobutyl (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C50 H44 Cl N7 O12
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

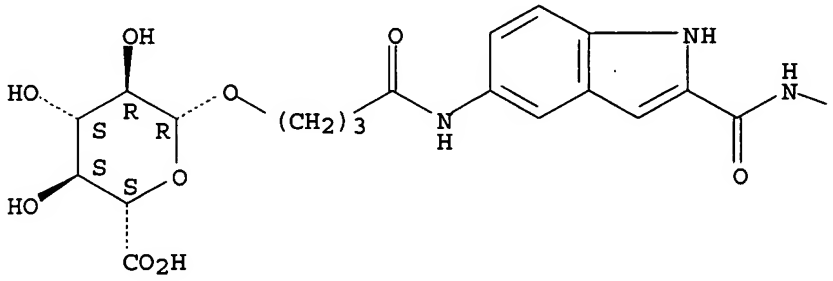
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:48468

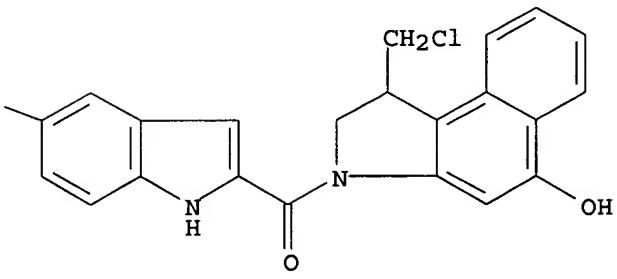
L26 ANSWER 73 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 199806-64-9 REGISTRY
CN β-D-Glucopyranosiduronic acid, 4-[[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]-4-oxobutyl (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C41 H38 Cl N5 O11
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

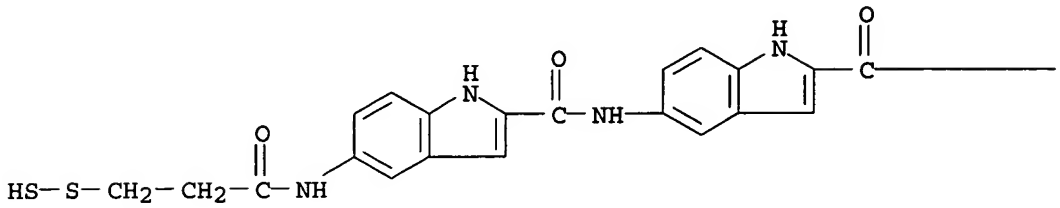
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:48468

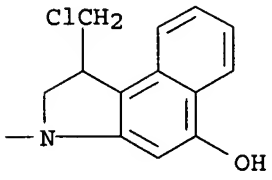
L26 ANSWER 74 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 199806-62-7 REGISTRY
CN 1-Propanesulfenothioic acid, 3-[[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]-3-oxo- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C34 H28 Cl N5 O4 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

DT.CA CAplus document type: Patent
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

PAGE 1-A



PAGE 1-B



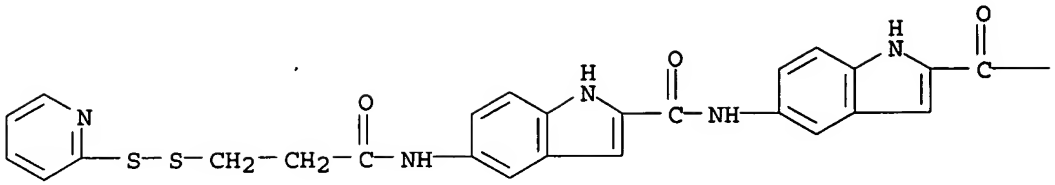
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

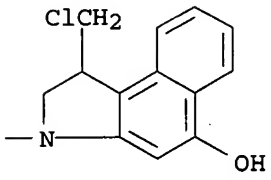
REFERENCE 1: 128:48468

L26 ANSWER 75 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 199806-61-6 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[[1-oxo-3-(2-pyridinyldithio)propyl]amino]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C39 H31 Cl N6 O4 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

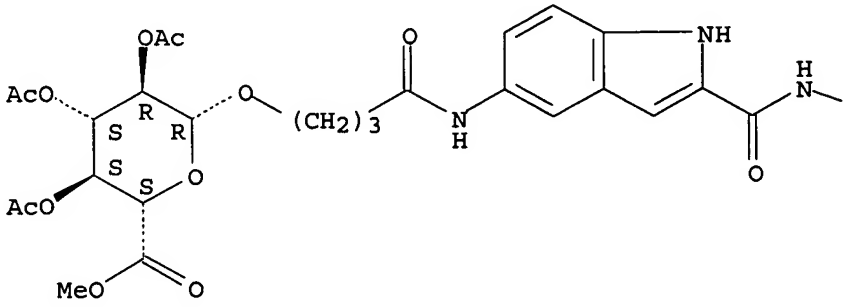
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:48468

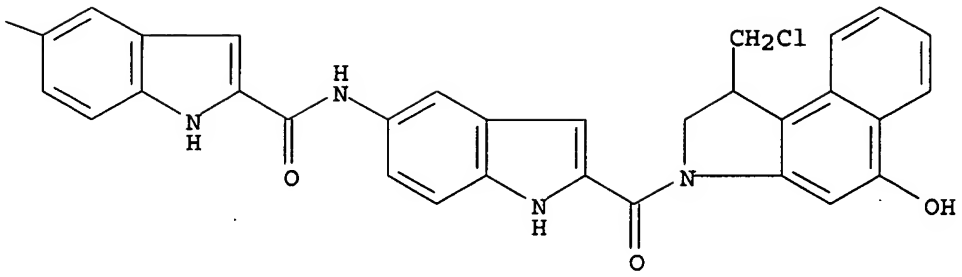
L26 ANSWER 76 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 199806-42-3 REGISTRY
CN β-D-Glucopyranosiduronic acid, 4-[[2-[[[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]-4-oxobutyl, methyl ester, 2,3,4-triacetate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C57 H52 Cl N7 O15
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

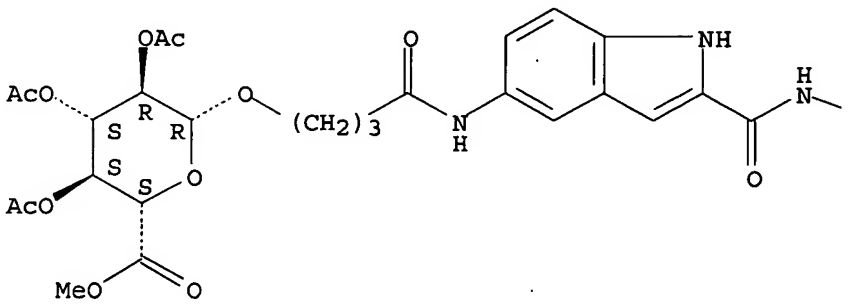
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:48468

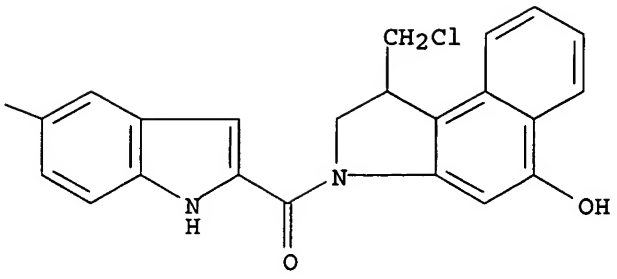
L26 ANSWER 77 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 199806-41-2 REGISTRY
CN β-D-Glucopyranosiduronic acid, 4-[[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]-4-oxobutyl, methyl ester, 2,3,4-triacetate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C48 H46 Cl N5 O14
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

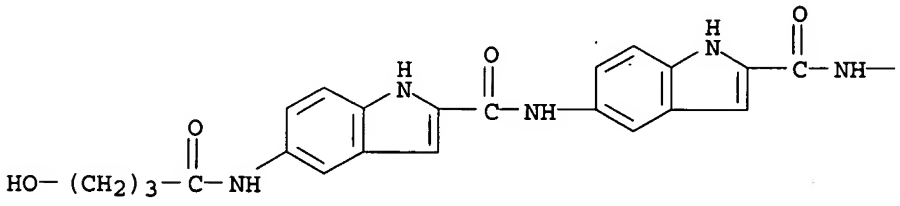
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:127387

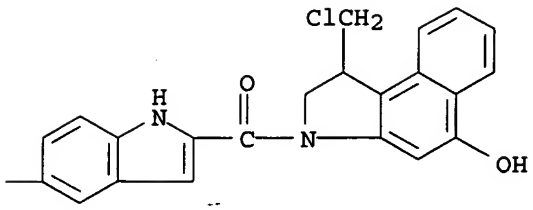
REFERENCE 2: 128:48468

L26 ANSWER 78 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 199806-39-8 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]-5-[(4-hydroxy-1-oxobutyl)amino]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C44 H36 Cl N7 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

PAGE 1-A



PAGE 1-B



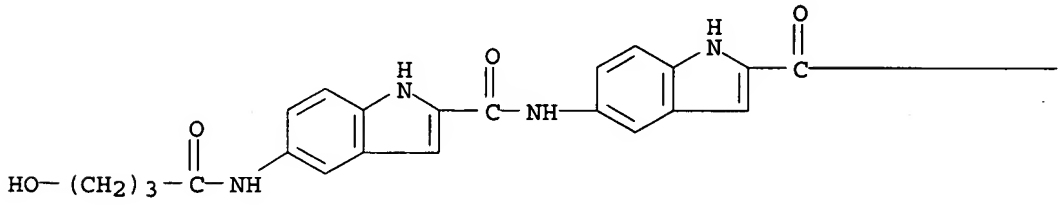
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:48468

L26 ANSWER 79 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 199806-38-7 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(4-hydroxy-1-oxobutyl)amino]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C35 H30 Cl N5 O5
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

PAGE 1-A



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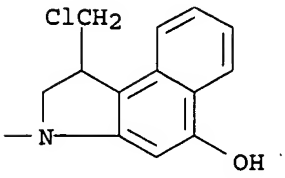


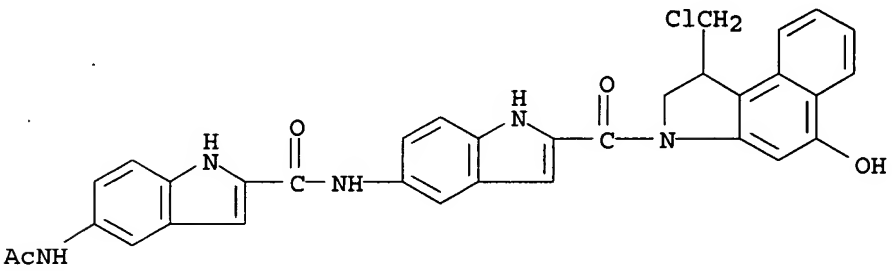
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:127387

REFERENCE 2: 128:48468

L26 ANSWER 80 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 199806-33-2 REGISTRY
CN 1H-Indole-2-carboxamide, 5-(acetylamino)-N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C33 H26 Cl N5 O4
SR CA
LC STN Files: CA, CAPLUS, PROUSDDR, SYNTHLINE, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

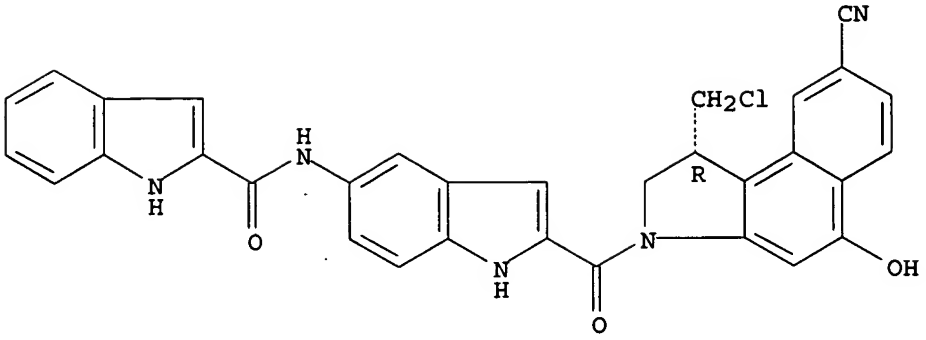
REFERENCE 1: 138:204856

REFERENCE 2: 132:321743

REFERENCE 3: 128:48468

L26 ANSWER 81 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 178877-34-4 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-8-cyano-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H22 Cl N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

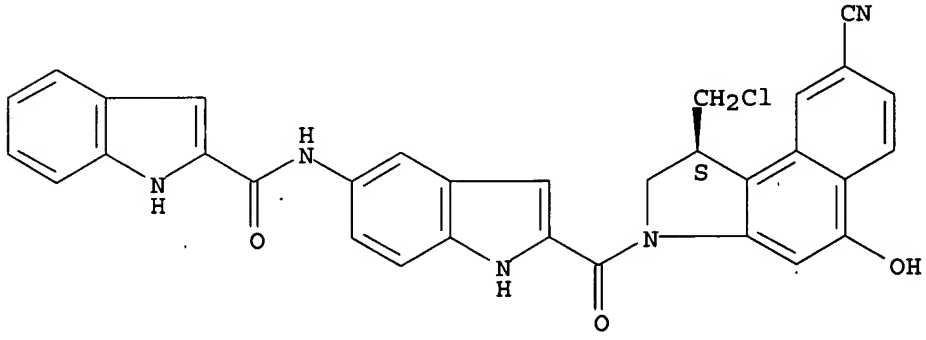
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:61379

REFERENCE 2: 125:114357

L26 ANSWER 82 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 178877-33-3 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-8-cyano-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H22 Cl N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry. Rotation (+).



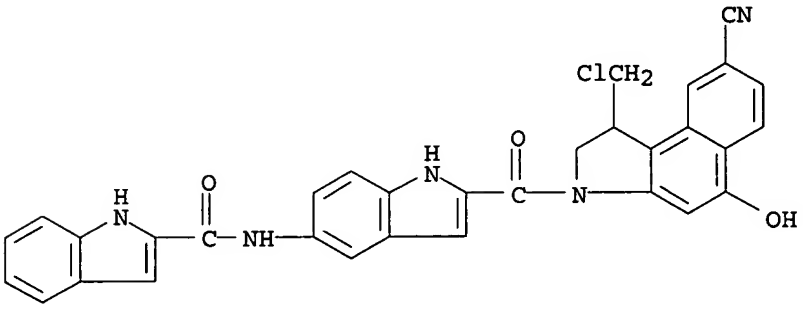
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:61379

REFERENCE 2: 125:114357

L26 ANSWER 83 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 178877-22-0 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-8-cyano-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C32 H22 Cl N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 125:114357

L26 ANSWER 84 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 173483-79-9 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-8-methoxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H25 Cl N4 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry. Rotation (-).